

09/897465

(FILE 'REGISTRY' ENTERED AT 11:27:20 ON 10 JAN 2003)

L1 277 SEA FILE=REGISTRY ABB=ON PLU=ON CC..P.C[7.]C|GCCSLPPCAL
NNPDYC/SQSP
L9 87 SEA FILE=REGISTRY ABB=ON PLU=ON L1 AND SQL=<17

FILE 'HCAPLUS' ENTERED AT 11:25:31 ON 10 JAN 2003

L1 277 SEA FILE=REGISTRY ABB=ON PLU=ON CC..P.C[7.]C|GCCSLPPCAL
NNPDYC/SQSP
L9 87 SEA FILE=REGISTRY ABB=ON PLU=ON L1 AND SQL=<17
L10 54 SEA FILE=HCAPLUS ABB=ON PLU=ON L9
L12 45 SEA FILE=HCAPLUS ABB=ON PLU=ON L10(L)ALPHA CONOTOXIN

L12 ANSWER 1 OF 45 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2002:777965 HCAPLUS

DOCUMENT NUMBER: 137:289027

TITLE: Alpha conotoxin peptides with analgesic
propertiesINVENTOR(S): Livett, Bruce; Khalil, Zeinab; Gayler, Kenwyn;
Down, John

PATENT ASSIGNEE(S): Australia

SOURCE: PCT Int. Appl., 87 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002079236	A1	20021010	WO 2002-AU411	20020328
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			

PRIORITY APPLN. INFO.: AU 2001-4094 A 20010329

OTHER SOURCE(S): MARPAT 137:289027

AB This invention relates to novel .alpha.-conotoxin-like peptides comprising the following sequence of amino acids:
Xaa1CCSXaa2Xaa3Xaa4CXaa5Xaa6Xaa7Xaa8Xaa9Xaa10Xaa11C-NH2 in which Xaa1 is G or D; Xaa3 is proline, hydroxyproline or glutamine; each of Xaa2 to Xaa8 and Xaa11 is independently any amino acid; Xaa9 is proline, hydroxyproline or glutamine; Xaa10 is aspartate, glutamate or .gamma.-carboxyglutamate; Xaa11 is optionally absent; and the C-terminus is optionally amidated, with the proviso that the peptide is not .alpha.-conotoxin Epl or .alpha.-conotoxin Iml. The peptides are useful in the treatment or prevention of pain, in recovery from nerve injury, and in the treatment of painful neurol. conditions such as stroke.

IT 467428-30-4 467428-33-7

RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological

Searcher : Shears 308-4994

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study); USES (Uses)

(.alpha.-conotoxin peptides with analgesic properties)

REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 2 OF 45 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2002:520404 HCAPLUS

DOCUMENT NUMBER: 137:226853

TITLE: Methylyllycaconitine is a potent antagonist of .alpha.-conotoxin-MII-sensitive presynaptic nicotinic acetylcholine receptors in rat striatum

AUTHOR(S): Mogg, Adrian J.; Whiteaker, Paul; McIntosh, J. Michael; Marks, Michael; Collins, Allan C.; Wonnacott, Susan

CORPORATE SOURCE: Department of Biology and Biochemistry, University of Bath, Bath, UK

SOURCE: Journal of Pharmacology and Experimental Therapeutics (2002), 302(1), 197-204
CODEN: JPETAB; ISSN: 0022-3565

PUBLISHER: American Society for Pharmacology and Experimental Therapeutics

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The plant alkaloid methylyllycaconitine (MLA) is considered to be a selective antagonist of the .alpha.7 subtype of neuronal nicotinic acetylcholine receptor (nAChR). However, 50 nM MLA partially inhibited (by 16%) [3H]dopamine release from rat striatal synaptosomes stimulated with 10 .mu.M nicotine. Other .alpha.7-selective antagonists had no effect. Similarly, MLA (50 nM) inhibited [3H]dopamine release evoked by the partial agonist (2-chloro-5-pyridyl)-9-azabicyclo[4.2.1]non-2-ene (UB-165) (0.2 .mu.M) by 37%. In both cases, inhibition by MLA was surmountable with higher agonist concns., indicative of a competitive interaction. At least two subtypes of presynaptic nAChR can modulate dopamine release in the striatum, and these nAChR are distinguished by their differential sensitivity to .alpha.-conotoxin-MII (.alpha.-CTx-MII). MLA was not additive with a maximally effective concn. of .alpha.-CTx-MII (100 nM) in inhibiting [3H]dopamine release elicited by 10 .mu.M nicotine or 0.2 .mu.M UB-165, suggesting that both toxins act at the same site. This was confirmed in quant. binding assays with 125I-.alpha.-CTx-MII, which displayed saturable specific binding to rat striatum and nucleus accumbens with Bmax values of 9.8 and 16.5 fmol/mg of protein, and Kd values of 0.63 and 0.83 nM, resp. MLA fully inhibited 125I-.alpha.-CTx-MII binding to striatum and nucleus accumbens with a Ki value of 33 nM, consistent with the potency obsd. in the functional assays. The authors speculate that MLA and .alpha.-CTx-MII interact with a presynaptic nAChR of subunit compn. .alpha.3/.alpha.6.beta.2.beta.3* on dopamine neurons. The use of MLA as an .alpha.7-selective antagonist should be exercised with caution, esp. in studies of nAChR in basal ganglia.

IT 175735-93-0, .alpha.-Conotoxin-MII

RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)

(methylyllycaconitine antagonism of .alpha.-

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conotoxin-MII-sensitive presynaptic nicotinic receptors
in dopamine release regulation in rat striatum)

REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE
FOR THIS RECORD. ALL CITATIONS AVAILABLE
IN THE RE FORMAT

L12 ANSWER 3 OF 45 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2002:509427 HCAPLUS

TITLE: The synthesis and structure of an n-terminal
dodecanoic acid conjugate of .alpha.-conotoxin
MII

AUTHOR(S): Blanchfield, Joanne; Dutton, Julie; Hogg, Ron;
Craik, David; Adams, David; Lewis, Richard;
Alewood, Paul; Toth, Istvan

CORPORATE SOURCE: School of Pharmacy, The University of
Queensland, Brisbane, Australia

SOURCE: Letters in Peptide Science (2002), Volume Date
2001, 8(3-5), 235-239

CODEN: LPSCEM; ISSN: 0929-5666

PUBLISHER: Kluwer Academic Publishers

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The .alpha.-conotoxin MII is a 16 amino acid long peptide toxin
isolated from the marine snail, Conus magus. This toxin has been
found to be a highly selective and potent inhibitor of neuronal
nicotinic acetylcholine receptors of the subtype .alpha.3.beta.2.
To improve the bioavailability of this peptide, the authors have
coupled 2-amino-DL-dodecanoic acid to the N-terminus of conotoxin
MII creating a lipidic linear peptide, which was then successfully
oxidized to produce the correctly folded conotoxin MII construct.

IT 186420-62-2P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);
RACT (Reactant or reagent)

(prepn. of an aminododecanoic acid conjugate of .alpha.
-conotoxin MII)

IT 175735-93-0P

RL: SPN (Synthetic preparation); PREP (Preparation)

(prepn. of an aminododecanoic acid conjugate of .alpha.
-conotoxin MII)

REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE
FOR THIS RECORD. ALL CITATIONS AVAILABLE
IN THE RE FORMAT

L12 ANSWER 4 OF 45 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2002:458936 HCAPLUS

DOCUMENT NUMBER: 137:273401

TITLE: Differential nicotinic receptor expression in
monkey basal ganglia: Effects of nigrostriatal
damage

AUTHOR(S): Quik, M.; Polonskaya, Y.; McIntosh, J. M.;
Kulak, J. M.

CORPORATE SOURCE: The Parkinson's Institute, Sunnyvale, CA, 94089,
USA

SOURCE: Neuroscience (Oxford, United Kingdom) (2002),
112(3), 619-630

CODEN: NRSCDN; ISSN: 0306-4522

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

Searcher : Shears 308-4994

LANGUAGE: English

AB The authors' previous work showed that there were marked declines in 125I-.alpha.-conotoxin MII labeled nicotinic receptors in monkey basal ganglia after nigrostriatal damage, findings that suggest .alpha.3/.alpha.6 contg. nicotinic receptors sites may be of relevance to Parkinson's disease. The authors now investigate whether there are differential changes in the distribution pattern of nicotinic receptor subtypes in the basal ganglia in 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP)-lesioned animals compared to controls to better understand the changes occurring with nigrostriatal damage. To approach this the authors used 125I-.alpha.-conotoxin MII, a marker for .alpha.3/.alpha.6 nicotinic receptors, and 125I-epibatidine, a ligand that labels multiple nicotinic subtypes. The results demonstrate that there were medial to lateral gradients in nicotinic receptor distribution in control striatum, as well as ventromedial to dorsolateral gradients in the substantia nigra, which resembled those of the dopamine transporter in these same brain regions. Treatment with MPTP, a neurotoxin that selectively destroys dopaminergic nigrostriatal neurons, led to a relatively uniform decrease in nicotinic receptor sites in the striatum, but a differential effect in the substantia nigra with significantly greater declines in the ventrolateral portion. Competition anal. in the striatum showed that .alpha.-conotoxin MII sensitive sites were primarily affected after lesioning, whereas multiple nicotinic receptor populations were decreased in the substantia nigra. From these data the authors suggest that in the striatum .alpha.3/.alpha.6 nicotinic receptors are primarily localized on dopaminergic nerve terminals, while multiple nicotinic receptor subtypes are present on dopaminergic cell bodies in the substantia nigra. Thus, if activation of striatal nicotinic receptors is key in the regulation of basal ganglia function, .alpha.3/.alpha.6-directed nicotinic receptor ligands may be more relevant for Parkinson's disease therapy. However, nicotinic receptor ligands with a broader specificity may be more important if receptors in the substantia nigra play a dominant role in controlling nigrostriatal activity.

IT 175735-93-0, .alpha.-Conotoxin MII

RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(nicotinic receptor ligand; differential nicotinic receptor expression in monkey basal ganglia and effects of nigrostriatal damage)

REFERENCE COUNT: 68 THERE ARE 68 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 5 OF 45 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2002:449219 HCAPLUS

DOCUMENT NUMBER: 138:540

TITLE: Characterization of [125I]epibatidine binding and nicotinic agonist-mediated 86Rb+ efflux in interpeduncular nucleus and inferior colliculus of .beta.2 null mutant mice

AUTHOR(S): Marks, Michael J.; Whiteaker, Paul; Grady, Sharon R.; Picciotto, Marina R.; McIntosh, J. Michael; Collins, Allan C.

CORPORATE SOURCE: Institute for Behavioral Genetics, University of Colorado, Boulder, CO, 80309-0447, USA

09/897465

SOURCE: Journal of Neurochemistry (2002), 81(5),
1102-1115
CODEN: JONRA9; ISSN: 0022-3042
PUBLISHER: Blackwell Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The .beta.2 nicotinic acetylcholine receptor subunit null mutation eliminated most high affinity [3H]epibatidine binding in mouse brain, but significant binding remained in accessory olfactory nucleus, medial habenula, inferior colliculus and interpeduncular nucleus. Residual [125I]epibatidine binding sites in the inferior colliculus and interpeduncular nucleus were subsequently characterized. Inhibition of [125I]epibatidine binding by 12 agonists and six antagonists was very similar in these regions. Most acetylcholine-stimulated 86Rb+ efflux is eliminated in thalamus and superior colliculus of .beta.2 null mutants, but significant activity remained in inferior colliculus and interpeduncular nucleus. This residual activity was subsequently characterized. The 12 nicotinic agonists tested elicited concn.-dependent 86Rb+ efflux. Epibatidine was the most potent agonist. Cytisine was also potent and efficacious. EC50 values for quaternary agonists were relatively high. Cytisine-stimulated 86Rb+ efflux was inhibited by six classical nicotinic antagonists. Mecamylamine and D-tubocurarine were most potent, while decamethonium was the least potent. Agonists and antagonists exhibited similar potency in both brain regions. .alpha.-Bungarotoxin (100 nM) did not significantly inhibit cytisine-stimulated 86Rb+ efflux, while the .alpha.3.beta.4 selective antagonist, .alpha.ConotoxinAuIB, inhibited a significant fraction of the response in both brain regions. Thus, .beta.2 null mutant mice express residual nicotinic activity with properties resembling those of .alpha.3.beta.4*-nAChR.

IT 175735-93-0, .alpha.-Conotoxin MII
RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(characterization of [125I]epibatidine binding and nicotinic agonist-mediated 86Rb+ efflux in interpeduncular nucleus and inferior colliculus of .beta.2 null mutant mice)

REFERENCE COUNT: 62 THERE ARE 62 CITED REFERENCES AVAILABLE
FOR THIS RECORD. ALL CITATIONS AVAILABLE
IN THE RE FORMAT

L12 ANSWER 6 OF 45 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2002:324056 HCAPLUS

DOCUMENT NUMBER: 137:59609

TITLE: 5-Iodo-A-85380 binds to .alpha.-conotoxin
MII-sensitive nicotinic acetylcholine receptors
(nAChRs) as well as .alpha.4.beta.2* subtypes

AUTHOR(S): Kulak, Jennifer M.; Sum, Jocelyn; Musachio, John
L.; McIntosh, J. Michael; Quik, Maryka

CORPORATE SOURCE: The Parkinson's Institute, Sunnyvale, CA,
94089-1605, USA

SOURCE: Journal of Neurochemistry (2002), 81(2), 403-406
CODEN: JONRA9; ISSN: 0022-3042

PUBLISHER: Blackwell Publishing Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Recent work suggests that 5-iodo-A-85380, a radioiodinated analog of
the 3-pyridyl ether A-85380, represents a promising imaging agent

Searcher : Shears 308-4994

for non-invasive, in vivo studies of .alpha.4.beta.2* nicotinic acetylcholine receptors (nAChRs; *denotes receptors contg. the indicated subunits), because of its low non-specific binding, low in vivo toxicity and high selectivity for .alpha.4.beta.2* nAChRs. As an approach to elucidate nAChR subtypes expressed in striatum, we carried out competitive autoradiog. in monkey and rat brain using 5-[125I]iodo-A-85380 ([125I]A-85380) and [125I].alpha.-conotoxin MII, a ligand that binds with high affinity to .alpha.6* and .alpha.3* nAChRs, but not to .alpha.4.beta.2* nAChRs. Although A-85380 is reported to be selective for .alpha.4.beta.2* nAChRs, we obsd. that A-85380 completely inhibited [125I].alpha.-conotoxin MII binding in rat striatum and that A-85380 blocked >90% of [125I].alpha.-conotoxin MII sites in monkey caudate and putamen. These results suggest that A-85380 binds to non-.alpha.4.beta.2* nAChRs, including putative .alpha.6* nAChRs. Expts. to det. the percentage of [125I]A-85380 sites that contain .alpha.-conotoxin MII-sensitive (.alpha.6.beta.2*) nAChRs indicate that they represent about 10% of [125I]A-85380 sites in rodent striatum and about 30% of sites in monkey caudate and putamen. These data are important for identifying alterations in nicotinic receptor subtypes in Parkinson's disease and other basal ganglia disorders both in in vitro and in in vivo imaging studies.

IT 175735-93-0, .alpha.-Conotoxin MII

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(5-iodo-A-85380 binds to .alpha.-conotoxin
MII-sensitive nicotinic acetylcholine receptors)

REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE
FOR THIS RECORD. ALL CITATIONS AVAILABLE
IN THE RE FORMAT

L12 ANSWER 7 OF 45 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2002:259386 HCAPLUS

DOCUMENT NUMBER: 136:396263

TITLE: Involvement of the .alpha.3 subunit in central
nicotinic binding populations

AUTHOR(S): Whiteaker, Paul; Peterson, Cyrus G.; Xu, Wei;
McIntosh, J. Michael; Paylor, Richard; Beaudet,
Arthur L.; Collins, Allan C.; Marks, Michael J.

CORPORATE SOURCE: Inst. for Behavioral Genetics, Univ. of
Colorado, Boulder, CO, 80309, USA

SOURCE: Journal of Neuroscience (2002), 22(7), 2522-2529
CODEN: JNRSDS; ISSN: 0270-6474

PUBLISHER: Society for Neuroscience

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The .alpha.3 subunit gene was one of the first neuronal nicotinic acetylcholine receptor (nAChR) subunits to be cloned (Boulter et al., 1986), but direct evidence of .alpha.3 subunit contributions to mammalian central nAChR populations has not been presented. The studies reported here used mice engineered to contain a null mutation in the .alpha.3 nAChR subunit gene (Xu et al., 1999) to examine the involvement of the .alpha.3 subunit in central nAChR populations. Heterologously expressed .alpha..beta..beta.2 and .alpha..beta..beta.4 nAChRs are pharmacol. similar to native [125I].alpha.-conotoxin MII (.alpha.-CtxMII)-binding and A 85380-resistant [125I]epibatidine-binding nAChR subtypes nAChRs was tested using quant. autoradiog. in .alpha.3-null mutant mice. Somewhat surprisingly, deletion of the .alpha.3 nAChR subunit gene

did not affect expression of the great majority of [125I].alpha.-CtxMII-binding sites, indicating that they do not correspond to heterologously expressed .alpha.3.beta.2 nAChRs. The only exception to this was obsd. in the habenulointerpeduncular tract, where .alpha.3-dependent [125I].alpha.-CtxMII binding was obsd. This finding may suggest the presence of an addnl., minor nicotinic population in this pathway. In contrast, most A 85380-resistant [125I]epibatidine-binding nAChRs were dependent on .alpha.3 gene expression, suggesting that they do indeed correspond to an .alpha.3 nAChR subtype. However, widespread but lower levels of .alpha.3-independent A 85380-resistant [125I]epibatidine binding were also seen. Again, this may indicate the existence of an addnl., minor population of non-.alpha.3 A 85380-resistant sites.

IT 175735-93-0, .alpha.-Conotoxin MII

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(nicotinic receptor characterization in brain of nicotinic
receptor .alpha.3-subunit knockout mice)

REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE
FOR THIS RECORD. ALL CITATIONS AVAILABLE
IN THE RE FORMAT

L12 ANSWER 8 OF 45 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2002:211177 HCAPLUS

DOCUMENT NUMBER: 137:76110

TITLE: A novel choline-sensitive nicotinic receptor
subtype that mediates enhanced GABA release in
the chick ventral lateral geniculate nucleus

AUTHOR(S): Guo, J.-Z.; Chiappinelli, V. A.

CORPORATE SOURCE: Department of Pharmacology, The George
Washington University, School of Medicine and
Health Sciences, Washington, DC, 20037, USA

SOURCE: Neuroscience (Oxford, United Kingdom) (2002),
110(3), 505-513

CODEN: NRSCDN; ISSN: 0306-4522

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB We describe a novel choline-sensitive nicotinic receptor that
mediates enhanced GABA release in the chick ventral lateral
geniculate nucleus. Whole-cell recordings in slices demonstrated
that choline (0.03-10 mM), generally considered an
.alpha.7-selective agonist, and carbachol (3-300 .mu.M), a
non-selective cholinergic agonist, both increased the frequency of
spontaneous GABAergic events in ventral lateral geniculate nucleus
neurons. Tetrodotoxin (0.5 .mu.M) partially reduced responses to
carbachol, but eliminated responses to choline. During long-term (5
min) exposure to choline the GABA enhancement was maintained until
choline was washed out. Choline (300 .mu.M) enhanced the frequency
of spontaneous GABAergic events by 4.28-fold in control artificial
cerebrospinal fluid. This choline-mediated enhancement was
significantly reduced by the following nicotinic receptor
antagonists: 1 .mu.M dihydro-.beta.-erythroidine (1.49-fold
increase), 1 .mu.M methyllycaconitine (1.53-fold), and 0.2 .mu.M
.alpha.-conotoxin ImI (1.84-fold). In contrast, no significant
change was seen in the presence of 0.1 .mu.M dihydro-.beta.-
erythroidine, 0.1 .mu.M methyllycaconitine, 0.1 .mu.M
.alpha.-bungarotoxin, 0.1 .mu.M .alpha.-conotoxin MII, 0.1 .mu.M
.kappa.-bungarotoxin, or 1 .mu.M .alpha.-conotoxin AuIB. These

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results indicate that choline, at concns. as low as 100 .mu.M, activates a nicotinic receptor that is distinct from the classical 7 nicotinic receptors previously known to be activated by choline.

IT 175735-93-0, .alpha.-Conotoxin MII

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(novel choline-sensitive nicotinic receptor subtype mediates GABA release in chick embryo ventral lateral geniculate nucleus)

REFERENCE COUNT: 50 THERE ARE 50 CITED REFERENCES AVAILABLE
FOR THIS RECORD. ALL CITATIONS AVAILABLE
IN THE RE FORMAT

L12 ANSWER 9 OF 45 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2002:5325 HCAPLUS

DOCUMENT NUMBER: 136:65411

TITLE: Loss of nicotinic receptors in monkey striatum
after 1-methyl-4-phenyl-1,2,3,6-
tetrahydropyridine treatment is due to a decline
in .alpha.-conotoxin MII sites

AUTHOR(S): Kulak, Jennifer M.; McIntosh, J. Michael; Quik,
Maryka

CORPORATE SOURCE: The Parkinson's Institute, Sunnyvale, CA, USA
SOURCE: Molecular Pharmacology (2002), 61(1), 230-238

CODEN: MOPMA3; ISSN: 0026-895X

PUBLISHER: American Society for Pharmacology and
Experimental Therapeutics

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Nicotinic acetylcholine receptors (nAChRs) in the basal ganglia are a potential target for new therapeutics for Parkinson's disease. As an approach to detect expression of nAChRs in monkeys, we used 125I-epibatidine, an agonist at nAChRs contg. .alpha.2 to .alpha.6 subunits. 125I-Epibatidine binding sites are expressed throughout the control monkey brain, including the basal ganglia. The .alpha.3/.alpha.6-selective antagonist .alpha.-conotoxin MII maximally inhibited 50% of binding in the caudate-putamen and had no effect on 125I-epibatidine binding in the frontal cortex or thalamus. In contrast, inhibition expts. with nicotine, cytisine, and 3-(2(S)-azetidinylmethoxy)pyridine.cntdot.2HCl (A85380) showed a complete block of 125I-epibatidine binding in all regions investigated and did not discriminate between the .alpha.-conotoxin MII-sensitive and -insensitive populations in the striatum. To assess the effects of nigrostriatal damage, monkeys were rendered parkinsonian with the dopaminergic neurotoxin 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP). Animals with moderate striatal damage (dopamine transporter levels .apprx.30% of control) had a 40 to 50% decrease in 125I-epibatidine binding. Inhibition studies showed that the decrease in epibatidine binding was due to loss of .alpha.-conotoxin MII-sensitive nAChRs. Monkeys with severe nigrostriatal damage (dopamine transporter levels .ltoreq.5% of control) exhibited a 55 to 60% decrease in 125I-epibatidine binding, which seemed to be due to a complete loss of .alpha.-conotoxin MII nAChRs and a partial loss of other nAChR subtypes. These results show that nAChRs expressed in the primate striatum have similar affinities for nicotine, cytisine, and A85380, that .alpha.-conotoxin MII discriminates between nAChR populations in the caudate and putamen, and that .alpha.-conotoxin MII-sensitive nAChRs are selectively decreased after MPTP-induced nigrostriatal damage.

IT 175735-93-0, .alpha.-Conotoxin MII

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RL: ADV (Adverse effect, including toxicity); ARG (Analytical reagent use); ANST (Analytical study); BIOL (Biological study); USES (Uses)

(nicotinic receptors loss in monkey striatum after 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine treatment is due to a decline in .alpha.-conotoxin MII sites)

REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 10 OF 45 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2001:549336 HCAPLUS

DOCUMENT NUMBER: 135:271222

TITLE: Vulnerability of 125I-.alpha.-conotoxin MII binding sites to nigrostriatal damage in monkey.

AUTHOR(S): Quik, Maryka; Polonskaya, Yelena; Kulak, Jennifer M.; McIntosh, J. Michael

CORPORATE SOURCE: The Parkinson's Institute, Sunnyvale, CA, 94089, USA

SOURCE: Journal of Neuroscience (2001), 21(15), 5494-5500

CODEN: JNRSDS; ISSN: 0270-6474

PUBLISHER: Society for Neuroscience

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Parkinson's disease, a neurodegenerative movement disorder characterized by selective degeneration of nigrostriatal dopaminergic neurons, affects .apprx.1% of the population over 50. Because nicotinic acetylcholine receptors (nAChRs) may represent an important therapeutic target for this disorder, we performed expts. to elucidate the subtypes altered with nigrostriatal damage in parkinsonian monkeys. For this purpose we used 125I-.alpha.-conotoxin MII (CtxMII), a relatively new ligand that identifies .alpha.3 and/or .alpha.6 subunits contg. nAChR subtypes. In brain from untreated monkeys, there was saturable 125I-.alpha.-CtxMII binding to a single population of high-affinity nicotinic sites (Kd = 0.9 nM), primarily localized in the visual, habenula-interpeduncular, and nigrostriatal-mesolimbic pathways. Administration of the selective dopaminergic neurotoxin 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine resulted in damage to the nigrostriatal system and parkinsonism. Autoradiog. anal. showed that 125I-.alpha.-CtxMII sites were selectively reduced (.gtoreq.99%) in the basal ganglia and that the lesion-induced decreases correlated well with declines in the dopamine transporter, a marker of dopaminergic neuron integrity. These findings may indicate that most or all of 125I-.alpha.-CtxMII-labeled nAChR subtypes in the basal ganglia are present on nigrostriatal dopaminergic neurons, in contrast to 125I-epibatidine sites. These data suggest that the development of ligands directed to nAChR subtypes contg. .alpha.3 and/or .alpha.6 subunits may yield a novel treatment strategy for parkinsonian patients with nigrostriatal dopaminergic degeneration.

IT 175735-93-0, .alpha.-conotoxin MII

RL: BPR (Biological process); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); PROC (Process); USES (Uses)

(vulnerability of 125I-.alpha.-conotoxin MII binding sites to nigrostriatal damage in monkey)

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REFERENCE COUNT: 57 THERE ARE 57 CITED REFERENCES AVAILABLE
FOR THIS RECORD. ALL CITATIONS AVAILABLE
IN THE RE FORMAT

L12 ANSWER 11 OF 45 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2001:402212 HCAPLUS

DOCUMENT NUMBER: 135:134897

TITLE: An .alpha.4.beta.4 nicotinic receptor subtype is
present in chick retina: identification,
characterization and pharmacological comparison
with the transfected .alpha.4.beta.4 and
.alpha.6.beta.4 subtypes

AUTHOR(S): Barabino, Benedetta; Vailati, Silvia; Moretti,
Milena; McIntosh, J. Michael; Longhi, Renato;
Clementi, Francesco; Gotti, Cecilia

CORPORATE SOURCE: Department of Experimental Medicine and
Pathology, La Sapienza University, Rome, Italy

SOURCE: Molecular Pharmacology (2001), 59(6), 1410-1417
CODEN: MOPMA3; ISSN: 0026-895X

PUBLISHER: American Society for Pharmacology and
Experimental Therapeutics

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Retina from 1-day-old chicks is a valuable tissue model for studying
neuronal nicotinic receptors because it expresses a large no. of the
developmentally regulated high-affinity [3H]epibatidine labeled
nicotinic receptors. Most of these receptors contain the .beta.4
subunit assocd. with different .alpha. subunits. Using a sequential
immunodepletion procedure with anti-.alpha.6, anti-.beta.3,
anti-.beta.2, and anti-.beta.4 antibodies, we purified an
.alpha.4.beta.4 nicotinic receptor subtype that accounts for
.apprx.20-25% of the high-affinity [3H]epibatidine labeled receptors
present in retina at that developmental time. Immunopptn. and
Western blotting expts. confirmed that the purified subtype contains
only the .alpha.4 and .beta.4 subunits. This receptor binds a no.
of agonists and the antagonist dihydro-.beta.-erythroidine with
nanomolar affinity, whereas it has micromolar affinity for the
.alpha.-conotoxin MII and methyllycaconitine toxins and other
nicotinic antagonists. Comparison of the pharmacol. profile of this
purified native subtype with that of the same subtype transiently
expressed in human BOSC23 cells showed that they have very similar
rank orders and abs. Ki values for several nicotinic drugs.
Finally, because chick retina expresses an .alpha.6.beta.4-contg.
subtype with a high affinity for the .alpha.-conotoxin MII, we used
native and transfected .alpha.4.beta.4 and .alpha.6.beta.4 subtypes
to investigate the relative contributions of the .alpha. and .beta.
subunits to this binding, and found that the .alpha.6 subunit detcs.
the high affinity for this toxin.

IT 175735-93-0, .alpha.-conotoxin MII

RL: BAC (Biological activity or effector, except adverse); BSU
(Biological study, unclassified); BIOL (Biological study)

(identification, characterization, and pharmacol. comparison of
.alpha.4.beta.4 nicotinic receptor in chick retina)

REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE
FOR THIS RECORD. ALL CITATIONS AVAILABLE
IN THE RE FORMAT

L12 ANSWER 12 OF 45 HCAPLUS COPYRIGHT 2003 ACS

Searcher : Shears 308-4994

09/897465

ACCESSION NUMBER: 2001:380120 HCAPLUS
DOCUMENT NUMBER: 135:137700
TITLE: An efficient synthetic scheme for natural
.alpha.-conotoxins and their analogues
AUTHOR(S): Zhmak, M. N.; Kasheverov, I. E.; Utkin, Yu. N.;
Tsetlin, V. I.; Vol'pina, O. M.; Ivanov, V. T.
CORPORATE SOURCE: Shemyakin-Ovchinnikov Institute of Bioorganic
Chemistry, Russian Academy of Sciences, Moscow,
117997, Russia
SOURCE: Russian Journal of Bioorganic Chemistry
(Translation of Bioorganicheskaya Khimiya)
(2001), 27(2), 67-71
CODEN: RJBCET; ISSN: 1068-1620
PUBLISHER: MAIK Nauka/Interperiodica
DOCUMENT TYPE: Journal
LANGUAGE: English

AB An efficient scheme for the synthesis of .alpha.-conotoxins, contg.
12-18 amino acid residues and two disulfide bridges, was proposed.
Its advantages are: (1) the avoidance of orthogonal protections of
Cys residues; (2) a lower no. of stages in a cycle of the peptide
chain elongation by the method of solid phase synthesis; (3) the
linear product is sufficiently pure for being used at the next stage
of the disulfide bond formation without addnl. purifn.; and (4) a
substantially reduced time of oxidn. to disulfides at pH 10, which
led to the target product in a high yield. A no. of natural
.alpha.-conotoxins (GI, ImI, EI, MII, and SIA), affecting the muscle
and neuronal nicotinic acetylcholine receptors of various types, and
several new analogs of these conotoxins (in particular, [Tyr10]ImI,
[Gln12]GI, and [Ser1]GI) were synthesized by this scheme. They were
used for elucidating the spatial structure of .alpha.-conotoxins by
1H NMR spectroscopy and for studying the ligand-binding sites of
their receptors.

IT 175735-93-0P, .alpha.-Conotoxin M II
RL: SPN (Synthetic preparation); PREP (Preparation)
(solid phase synthesis of natural **alpha**
conotoxins and their analogs)

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE
FOR THIS RECORD. ALL CITATIONS AVAILABLE
IN THE RE FORMAT

L12 ANSWER 13 OF 45 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2000:513711 HCAPLUS
DOCUMENT NUMBER: 133:131093
TITLE: Protein and cDNA sequences of Conus
.alpha.-conotoxins and the therapeutic uses
thereof as neuromuscular blocking agent
INVENTOR(S): Olivera, Baldomero M.; Layer, Richard T.;
Watkins, Maren; Hillyard, David R.; McIntosh, J.
Michael; Jones, Robert M.
PATENT ASSIGNEE(S): University of Utah Research Foundation, USA;
Cognetix, Inc.
SOURCE: PCT Int. Appl., 95 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

Searcher : Shears 308-4994

09/897465

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000043409	A2	20000727	WO 2000-US1372	20000121
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 2000027327	A5	20000807	AU 2000-27327	20000121
US 6268473	B1	20010731	US 2000-488799	20000121
EP 1159288	A1	20011205	EP 2000-905680	20000121
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

PRIORITY APPLN. INFO.: US 1999-116881P P 19990122
 US 1999-116882P P 19990122
 WO 2000-US1372 W 20000121

OTHER SOURCE(S): MARPAT 133:131093

AB The invention provides protein and cDNA sequences of Conus .alpha.-conotoxins. Conus .alpha.-conotoxins are relatively short peptides, about 10-25 residues in length, and are naturally available in minute amts. in the venom of the cone snails. The invention further relates to the therapeutic uses of the Conus .alpha.-conotoxins as neuromuscular blocking agents, such as muscle relaxants for treating benign essential blepharospasm and other forms of focal dystonia and for anti-wrinkle use.

IT 285558-22-7P 285558-23-8P 285558-24-9P
 RL: BOC (Biological occurrence); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation); USES (Uses)
 (protein and cDNA sequences of Conus .alpha.-conotoxins and therapeutic uses thereof as neuromuscular blocking agent)

L12 ANSWER 14 OF 45 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2000:303382 HCAPLUS

DOCUMENT NUMBER: 133:38562

TITLE: 125I-.alpha.-conotoxin MII identifies a novel nicotinic acetylcholine receptor population in mouse brain

AUTHOR(S): Whiteaker, Paul; McIntosh, J. Michael; Luo, Siqin; Collins, Allan C.; Marks, Michael J.

CORPORATE SOURCE: Institute for Behavioral Genetics, University of Colorado, Boulder, CO, USA

SOURCE: Molecular Pharmacology (2000), 57(5), 913-925
 CODEN: MOPMA3; ISSN: 0026-895X

PUBLISHER: American Society for Pharmacology and Experimental Therapeutics

DOCUMENT TYPE: Journal

LANGUAGE: English

AB .alpha.-Conotoxin MII (CtxMII), a peptide toxin from the venom of the predatory cone snail Conus magus, displays an unusual nicotinic pharmacol. Specific binding of a radioiodinated deriv. (125I-.alpha.-CtxMII) was identified in brain region homogenates and

tissue sections. Quant. autoradiog. indicated that 125I-.alpha.-CtxMII binding sites have an unique pharmacol. profile and distribution in mouse brain, being largely confined to the superficial layers of the superior colliculus, nigrostriatal pathway, optic tract, olivary pretectal, and mediolateral and dorsolateral geniculate nuclei. Expression of .alpha.-CtxMII binding sites in the nigrostriatal pathway, combined with evidence for .alpha.-CtxMII-sensitivity of nicotine-induced [3H]dopamine release in rodent striatal preps. indicates that 125I-.alpha.-CtxMII binding nicotinic acetylcholine receptors are likely to be physiol. important. Unlabeled .alpha.-CtxMII potently (Ki <3 nM) competed for a subset of [3H]epibatidine binding sites in mouse brain homogenates, but weakly (IC50 >10 .mu.M) interacted with 125I-.alpha.-bungarotoxin and (-)-[3H]nicotine binding sites, confirming this compd.'s novel nicotinic pharmacol. Quant. autoradiog. revealed that .alpha.-CtxMII binds with high affinity at a subset of [3H]epibatidine binding sites with relatively low cytisine affinity ("cytisine-resistant" sites), resolving [3H]epibatidine binding into three different populations, each probably corresponding to a receptor subtype. The majority population seems to correspond to that which binds nicotine and cytisine with high affinity ("cytisine-sensitive" sites). Comparison of the cytisine-resistant population's distribution with that of .alpha.3 subunit mRNA expression suggests that the fractions both more and less sensitive to .alpha.-CtxMII probably contain the .alpha.3 subunit, perhaps in combination with different .beta. subunits.

IT 175735-93-0, .alpha.-Conotoxin MII

RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(.alpha.-conotoxin MII-binding nicotinic acetylcholine receptor population in mouse brain and distribution and function and pharmacol. characterization thereof)

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 15 OF 45 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2000:256009 HCAPLUS

DOCUMENT NUMBER: 133:13021

TITLE: Conus peptides: novel probes for nicotinic acetylcholine receptor structure and function

AUTHOR(S): McIntosh, J. M.; Gardner, S.; Luo, S.; Garrett, J. E.; Yoshikami, D.

CORPORATE SOURCE: Department of Psychiatry, University of Utah, Salt Lake City, UT, USA

SOURCE: European Journal of Pharmacology (2000), 393(1-3), 205-208

CODEN: EJPHAZ; ISSN: 0014-2999

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Conus is a genus of predatory marine snails that uses venom to capture prey. Among the neurotoxins widely utilized by the cone snails are the .alpha.-conotoxins which are disulfide-rich peptides that target muscle or neuronal subtypes of nicotinic acetylcholine receptors. The small size and receptor subtype specificity of these

peptides make them particularly useful for characterizing both native and heterologously expressed nicotinic receptors. In this report, we demonstrate that .alpha.-conotoxin MII potently blocks .beta.3-contg. neuronal nicotinic receptors. Furthermore, initial evidence suggests that subpopulations of .alpha.3.beta.2.beta.3-contg. receptors are differentially sensitive to .alpha.-conotoxin MII. Thus, .alpha.-conotoxin MII promises to be a useful tool for studying neuronal nicotinic receptors contg. the .beta.3 subunit.

IT 175735-93-0, .alpha.-Conotoxin MII

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(Conus peptides as probes for nicotinic acetylcholine receptor structure and function)

REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 16 OF 45 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2000:255989 HCAPLUS

DOCUMENT NUMBER: 133:14832

TITLE: .beta.3 Subunit is present in different nicotinic receptor subtypes in chick retina

AUTHOR(S): Vailati, S.; Moretti, M.; Balestra, B.; McIntosh, M.; Clementi, F.; Gotti, C.

CORPORATE SOURCE: University of Milan, Department of Medical Pharmacology, CNR Cellular and Molecular Pharmacology Center, Milan, 20129, Italy

SOURCE: European Journal of Pharmacology (2000), 393(1-3), 23-30

CODEN: EJPHAZ; ISSN: 0014-2999

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Using subunit-specific antibodies and immunopptn. expts., we have identified the retina as being the chick central nervous system (CNS) area that expresses the highest level of the .beta.3 subunit. Sequential immunopurifn. expts. showed that there are .gtoreq.2 populations of .beta.3-contg. receptors in chick retina: in one, the .beta.3 subunit is assocd. with the .alpha.6 and .beta.4 subunits; in the other more heterogeneous population, the .beta.3 subunit is assocd. with the .alpha.2, .alpha.3, .alpha.4, .beta.2, and .beta.4 subunits. Both of these receptor populations bind [3H]epibatidine and a no. of nicotinic receptor agonists with high affinity (nM) and nicotinic receptor antagonists with a lower affinity (.mu.M). The greatest pharmacol. difference between the 2 populations is the affinity for the .alpha.-conotoxin MII, which inhibits binding to .alpha.6-contg. receptors and not that to .beta.3-contg. receptors. We also searched for the presence of the .beta.3 subunit assocd. with the .alpha.-bungarotoxin binding subunits .alpha.7 and/or .alpha.8 in retina and chick brain. Immunopptn. studies using anti-.beta.3 antibodies did not detect any specific .alpha.-bungarotoxin labeled receptors, thus, indicating that the .beta.3 subunit is not present in the .alpha.-bungarotoxin receptors of these areas.

IT 175735-93-0, .alpha.-Conotoxin M II

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)

09/897465

(.beta.3 subunit is present in different nicotinic receptor subtypes in chick retina)

REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 17 OF 45 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2000:243855 HCAPLUS

DOCUMENT NUMBER: 132:343676

TITLE: UB-165: A novel nicotinic agonist with subtype selectivity implicates the .alpha.4.beta.2* subtype in the modulation of dopamine release from rat striatal synaptosomes

AUTHOR(S): Sharples, Christopher G. V.; Kaiser, Sergio; Soliakov, Lev; Marks, Michael J.; Collins, Allan C.; Washburn, Mark; Wright, Emma; Spencer, James A.; Gallagher, Timothy; Whiteaker, Paul; Wonnacott, Susan

CORPORATE SOURCE: Department of Biology and Biochemistry, University of Bath, Bath, BA2 7AY, UK

SOURCE: Journal of Neuroscience (2000), 20(8), 2783-2791
CODEN: JNRSDS; ISSN: 0270-6474

PUBLISHER: Society for Neuroscience

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Presynaptic nicotinic acetylcholine receptors (nAChRs) on striatal synaptosomes stimulate dopamine release. Partial inhibition by the .alpha.3.beta.2-selective .alpha.-conotoxin-MII indicates heterogeneity of presynaptic nAChRs on dopamine terminals. We have used this .alpha.-conotoxin and UB-165, a novel hybrid of epibatidine and anatoxin-1, to address the hypothesis that the .alpha.-conotoxin-MII-insensitive subtype is composed of .alpha.4 and .beta.2 subunits. UB-165 shows intermediate potency, compared with the parent mols., at .alpha.4.beta.2* and .alpha.3-contg. binding sites, and resembles epibatidine in its high discrimination of these sites over .alpha.7-type and muscle binding sites. (.+-.)-Epibatidine, (.+-.)-anatoxin-a, and (.+-.)-UB-165 stimulated [3H]-dopamine release from striatal synaptosomes with EC50 values of 2.4, 134, and 88 nM, and relative efficacies of 1:0.4:0.2, resp. .alpha.-Conotoxin-MII inhibited release evoked by these agonists by 48, 56, and 88%, resp., suggesting that (.+-.)-UB-165 is a very poor agonist at the .alpha.-conotoxin-MII-insensitive nAChR subtype. In assays of 86Rb+ efflux from thalamic synaptosomes, a model of an .alpha.4.beta.2* nAChR response, (.+-.)-UB-165 was a very weak partial agonist; the low efficacy of (.+-.)-UB-165 at .alpha.4.beta.2 nAChR was confirmed in Xenopus oocytes expressing various combinations of human nAChR subunits. In contrast, (.+-.)-UB-165 and (.+-.)-anatoxin-a were similarly efficacious and similarly sensitive to .alpha.-conotoxin-MII in increasing intracellular Ca2+ in SH-SY5Y cells, a functional assay for native .alpha.3-contg. nAChR. These data support the involvement of .alpha.4.beta.2* nAChR in the presynaptic modulation of striatal dopamine release and illustrate the utility of exploiting a novel partial agonist, together with a selective antagonist, to dissect the functional roles of nAChR subtypes in the brain.

IT 175735-93-0, .alpha.-Conotoxin-MII

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)

Searcher : Shears 308-4994

09/897465

(UB-165 nicotinic agonist subtype selectivity implicates
.alpha.4.beta.2* subtype in modulation of dopamine release from
rat striatal synaptosomes)

REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE
FOR THIS RECORD. ALL CITATIONS AVAILABLE
IN THE RE FORMAT

L12 ANSWER 18 OF 45 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2000:191100 HCAPLUS

DOCUMENT NUMBER: 132:237373

TITLE: Preparation of cyclized conotoxin peptides

INVENTOR(S): Craik, David James; Daly, Norelle Lee; Nielsen,
Katherine Justine

PATENT ASSIGNEE(S): University of Queensland, Australia

SOURCE: PCT Int. Appl., 43 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000015654	A1	20000323	WO 1999-AU769	19990914
W:	AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
AU 9960705	A1	20000403	AU 1999-60705	19990914
AU 747006	B2	20020509		
EP 1129106	A1	20010905	EP 1999-947111	19990914
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO			

PRIORITY APPLN. INFO.: AU 1998-5895 A 19980914
WO 1999-AU769 W 19990914

AB Cyclized conotoxin peptides were prepd. for the therapeutic treatment of mammals. Thus, cyclo[CKGKGAKCSRLMYDCCTGSCRSKGKCTRNLPG], a cyclic analog of MVIIA having the linking moiety TRNLPG, was prepd. by the solid-phase method.

IT 175735-93-ODP, .alpha.-Conotoxin M II, cyclic analogs 195823-99-5DP, .alpha.-Conotoxin Pn IB, cyclic analogs 195824-00-1DP, .alpha.-Conotoxin Pn IA, cyclic analogs

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (prepn. of cyclized conotoxin peptides)

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR
THIS RECORD. ALL CITATIONS AVAILABLE IN
THE RE FORMAT

L12 ANSWER 19 OF 45 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2000:156025 HCAPLUS

DOCUMENT NUMBER: 132:318808

09/897465

TITLE: Leu10 of .alpha.-conotoxin PnIB confers potency for neuronal nicotinic responses in bovine chromaffin cells

AUTHOR(S): Broxton, N.; Miranda, L.; Gehrmann, J.; Down, J.; Alewood, P.; Livett, B.

CORPORATE SOURCE: Department of Biochemistry and Molecular Biology, University of Melbourne, Parkville, Australia

SOURCE: European Journal of Pharmacology (2000), 390(3), 229-236

CODEN: EJPHAZ; ISSN: 0014-2999

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Two .alpha.-conotoxins PnIA and PnIB (previously reported as being "mollusk specific") which differ in only two amino acid residues (AN vs. LS at residues 10 and 11, resp.), show markedly different inhibition of the neuronal nicotinic acetylcholine receptor response in bovine chromaffin cells, a mammalian prepn. Whereas .alpha.-conotoxin PnIB completely inhibits the nicotine-evoked catecholamine release at 10 .mu.M, with IC50 = 0.7 .mu.M, .alpha.-conotoxin PnIA is some 30-40 times less potent. Two peptide analogs, [A10L]PnIA and [N11S]PnIA were synthesized to investigate the extent to which each residue contributes to activity. [A10L]PnIA (IC50 = 2.0 .mu.M) completely inhibits catecholamine release at 10 .mu.M, whereas [N11S]PnIA shows little inhibition. In contrast, none of the peptides inhibit muscle-type nicotinic responses in the rat hemi-diaphragm prepn. The authors conclude that the enhanced potency of .alpha.-conotoxin PnIB over .alpha.-conotoxin PnIA in the neuronal-type nicotinic response is principally detd. by the larger, more hydrophobic leucine residue at position 10 in .alpha.-conotoxin PnIB.

IT 195823-99-5, .alpha.-Conotoxin PnIB
195824-00-1, .alpha.-Conotoxin PnIA

RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(Leu10 of .alpha.-conotoxin PnIB confers potency for neuronal nicotinic responses in bovine chromaffin cells)

REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 20 OF 45 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2000:148514 HCAPLUS

DOCUMENT NUMBER: 132:246458

TITLE: Pairwise interactions between neuronal .alpha.7 acetylcholine receptors and .alpha.-conotoxin PnIB

AUTHOR(S): Quiram, P. A.; McIntosh, J. M.; Sine, S. M.

CORPORATE SOURCE: Receptor Biology Laboratory, Department of Physiology and Biophysics Mayo Foundation, Rochester, MN, 55905, USA

SOURCE: Journal of Biological Chemistry (2000), 275(7), 4889-4896

CODEN: JBCHA3; ISSN: 0021-9258

PUBLISHER: American Society for Biochemistry and Molecular Biology

Searcher : Shears 308-4994

09/897465

DOCUMENT TYPE: Journal
LANGUAGE: English

AB This work uses .alpha.-conotoxin PnIB to probe the agonist binding site of neuronal .alpha.7 acetylcholine receptors. We mutated the 13 non-cysteine residues in CTx PnIB, expressed .alpha.7/5-hydroxytryptamine-3 homomeric receptors in 293 HEK cells, and measured binding of each mutant toxin to the expressed receptors by competition against the initial rate of 125I-.alpha.-bungarotoxin binding. The results reveal that residues Ser-4, Leu-5, Pro-6, Pro-7, Ala-9, and Leu-10 endow CTx PnIB with affinity for .alpha.7/5-hydroxytryptamine-3 receptors; side chains of these residues cluster in a localized region within the three-dimensional structure of CTx PnIB. We next mutated key residues in the seven loops of .alpha.7 that converge at subunit interfaces to form the agonist binding site. The results reveal predominant contributions by residues Trp-149 and Tyr-93 in .alpha.7 and smaller contributions by Ser-34, Arg-186, Tyr-188, and Tyr-195. To identify pairwise interactions that stabilize the receptor-conotoxin complex, we measured binding of receptor and toxin mutations and analyzed the results by double mutant cycles. The results reveal a single dominant interaction between Leu-10 of CTx PnIB and Trp-149 of .alpha.7 that anchors the toxin to the binding site. We also find weaker interactions between Pro-6 of CTx PnIB and Trp-149 and between both Pro-6 and Pro-7 and Tyr-93 of .alpha.7. The overall results demonstrate that a localized hydrophobic region in CTx PnIB interacts with conserved arom. residues on one of the two faces of the .alpha.7 binding site.

IT 195823-99-5, .alpha.-Conotoxin Pn IB
195824-00-1, .alpha.-Conotoxin Pn IA
221639-83-4 229639-63-8 263028-53-1
263028-54-2 263028-55-3 263028-56-4
263028-57-5 263028-58-6 263028-59-7
263028-61-1 263028-62-2 263028-63-3
263028-64-4 263028-65-5 263028-66-6
263028-67-7 263028-68-8 263028-69-9
263028-70-2 263028-71-3 263028-72-4
263028-73-5 263028-74-6 263028-75-7
263028-76-8 263028-77-9 263028-78-0
263028-79-1 263028-80-4 263028-81-5
263028-82-6 263028-83-7 263028-84-8

RL: BPR (Biological process); BSU (Biological study, unclassified);
PRP (Properties); BIOL (Biological study); PROC (Process)
(neuronal .alpha.7 acetylcholine receptor and .alpha.-
conotoxin PnIB pairwise interactions and
structure-activity relations therein)

REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE
FOR THIS RECORD. ALL CITATIONS AVAILABLE
IN THE RE FORMAT

L12 ANSWER 21 OF 45 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2000:2224 HCAPLUS

DOCUMENT NUMBER: 132:132466

TITLE: Single amino acid substitutions in
.alpha.-conotoxin PnIA shift selectivity for
subtypes of the mammalian neuronal nicotinic
acetylcholine receptor

AUTHOR(S): Hogg, Ron C.; Miranda, Les P.; Craik, David J.;
Lewis, Richard J.; Alewood, Paul F.; Adams,

Searcher : Shears 308-4994

CORPORATE SOURCE: David J.
The Department of Physiology and Pharmacology,
University of Queensland, Brisbane, 4072,
Australia
SOURCE: Journal of Biological Chemistry (1999), 274(51),
36559-36564
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular
Biology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The .alpha.-conotoxins, a class of nicotinic acetylcholine receptor (nAChR) antagonists, are emerging as important probes of the role played by different nAChR subtypes in cell function and communication. In this study, the native .alpha.-conotoxins PnIA and PnIB were found to cause concn.-dependent inhibition of the ACh-induced current in all rat parasympathetic neurons examd., with IC50 values of 14 and 33 nM, and a maximal redn. in current amplitude of 87% and 71%, resp. The modified .alpha.-conotoxin [N11S]PnIA reduced the ACh-induced current with an IC50 value of 375 nM and a maximally effective concn. caused 91% block. [A10L]PnIA was the most potent inhibitor, reducing the ACh-induced current in .apprx.80% of neurons, with an IC50 value of 1.4 nM and 46% maximal block of the total current. The residual current was not inhibited further by .alpha.-bungarotoxin, but was further reduced by the .alpha.-conotoxins PnIA or PnIB, and by mecamylamine. 1H NMR studies indicate that PnIA, PnIB, and the analogs, [A10L]PnIA and [N11S]PnIA, have identical backbone structures. The authors propose that positions 10 and 11 of PnIA and PnIB influence potency and det. selectivity among .alpha.7 and other nAChR subtypes, including .alpha.3.beta.2 and .alpha.3.beta.4. Four distinct components of the nicotinic ACh-induced current in mammalian parasympathetic neurons have been dissected with these conopeptides.

IT 195824-00-1, .alpha.-Conotoxin PnIA
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); USES (Uses)

(amino acid substitutions in .alpha.-conotoxin PnIA shift selectivity for subtypes of mammalian neuronal nicotinic acetylcholine receptor)

IT 195823-99-5, .alpha.-Conotoxin PnIB
221639-83-4 229639-63-8
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); USES (Uses)

(single amino acid substitutions in .alpha.-conotoxin PnIA shift selectivity for subtypes of mammalian neuronal nicotinic acetylcholine receptor)

REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 22 OF 45 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:649491 HCAPLUS
DOCUMENT NUMBER: 132:9825
TITLE: Single-Residue Alteration in .alpha.-Conotoxin

09/897465

AUTHOR(S): PnIA Switches Its nAChR Subtype Selectivity
Luo, S.; Nguyen, T. A.; Cartier, G. E.; Olivera,
B. M.; Yoshikami, D.; McIntosh, J. M.
CORPORATE SOURCE: Department of Biology, University of Utah, Salt
Lake City, UT, 84112, USA
SOURCE: Biochemistry (1999), 38(44), 14542-14548
CODEN: BICHAW; ISSN: 0006-2960
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB .alpha.-Conotoxins are disulfide-rich peptides that are competitive antagonists of nicotinic acetylcholine receptors (nAChRs). Despite their small size, different .alpha.-conotoxins are able to discriminate among different subtypes of mammalian nAChRs. In this report, the activity of two peptides from the venom of *Conus pennaceus*, .alpha.-conotoxins PnIA and PnIB, are examd. Although the toxins differ in only two residues, PnIA preferentially blocks .alpha.3.beta.2 nAChRs, whereas PnIB prefers the .alpha.7 subtype. Point mutation chimeras of these .alpha.-conotoxins were synthesized and their activities assessed on *Xenopus* oocytes expressing specific nAChRs. Change of a single residue, Ala10 to Leu, in PnIA (to form PnIA [A10L]) converts the parent peptide from .alpha.3.beta.2-preferring to .alpha.7-preferring; furthermore, PnIA [A10L] blocks the .alpha.7 receptor with an IC50 (12.6 nM) that is lower than that of either parent peptide. Kinetic anal. indicates that differences in affinity among the analogs are primarily due to differences in off-rate, with PnIA [A10L]'s interaction with .alpha.7 having the smallest off-rate (koff = 0.17 min⁻¹). Thermodyn. anal. indicates that Leu10 enhances the peptide's interaction with .alpha.7, but not .alpha.3.beta.2, receptors, whereas Ser11 (in PnIA [N11S]) reduces its affinity for both .alpha.7 and .alpha.3.beta.2 nAChRs.

IT 195824-00-1, .alpha.-Conotoxin PnIA
RL: BAC (Biological activity or effector, except adverse); BSU
(Biological study, unclassified); BIOL (Biological study)
(single-residue alteration in .alpha.-conotoxin
PnIA switches nAChR subtype selectivity)

IT 195823-99-5, .alpha.-Conotoxin PnIB
RL: BAC (Biological activity or effector, except adverse); BSU
(Biological study, unclassified); BIOL (Biological study)
(single-residue alteration in .alpha.-conotoxin
PnIA switches nAChR subtype selectivity in relation to PnIB)

REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE
FOR THIS RECORD. ALL CITATIONS AVAILABLE
IN THE RE FORMAT

L12 ANSWER 23 OF 45 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1999:468432 HCAPLUS
DOCUMENT NUMBER: 131:82983
TITLE: Uses of alpha-conotoxin peptides
INVENTOR(S): Olivera, Baldomero M.; McIntosh, J. Michael;
Yoshikami, Doju; Cartier, G. Edward; Luo, Siqin
PATENT ASSIGNEE(S): University of Utah Research Foundation, USA
SOURCE: PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9933482	A1	19990708	WO 1998-US27367	19981223
W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
AU 9920917	A1	19990719	AU 1999-20917	19981223
US 6265541	B1	20010724	US 1998-219446	19981223
US 2002022715	A1	20020221	US 2001-897465	20010703
PRIORITY APPLN. INFO.:			US 1997-70153P	P 19971231
			US 1998-80588P	P 19980403
			US 1998-219446	A3 19981223
			WO 1998-US27367	W 19981223

OTHER SOURCE(S): MARPAT 131:82983

AB The present invention relates to the use of .alpha.-conotoxin peptides having the general formula: Xaa1-Xaa2-Cys-Cys-Xaa3-Xaa4-Pro-Xaa5-Cys-Xaa6-Cys (SEQ ID NO.1) for treating disorders regulated at neuronal nicotinic acetylcholine receptors. Such disorders include, but are not limited to, cardiovascular disorders, gastric motility disorders, urinary incontinence, nicotine addiction, mood disorders (such as bipolar disorder, unipolar depression, dysthymia and seasonal effective disorder) and small cell lung carcinoma, as well as the localization of small cell lung carcinoma. In this formula, Xaa1 is des-Xaa1, Tyr, mono-iodo-Tyr or di-iodo-Tyr, Xaa2 is any amino acid, Xaa3 is any amino acid, Xaa4 is any amino acid, Xaa5 is any amino acid and Xaa6 represents a peptide of 3-7 amino acids. Disulfide linkages exist between the first and third cysteines and the second and fourth cysteines. Pro may be replaced with hydroxy-Pro. The C-terminus may contain a hydroxyl or an amide group, preferably an amide group.

IT 216299-20-6P, .alpha.-Conotoxin AuIA
 221639-83-4P 223416-43-1P, .alpha.-
 Conotoxin AuIC 229639-60-5P 229639-61-6P
 229639-63-8P 229639-64-9DP, radiolabeled
 229639-64-9P 229639-65-ODP, radiolabeled
 229639-65-0P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(uses of **alpha-conotoxin** peptides as
 nicotinic antagonists in relation to treatment neuronal nicotinic
 receptor disorders effect on neurotransmitter release)

IT 175735-93-0, .alpha.-Conotoxin MII
 195823-99-5, .alpha.-Conotoxin PnIB
 195824-00-1, .alpha.-Conotoxin PnIA
 229639-62-7

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(uses of **alpha-conotoxin** peptides as

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nicotinic antagonists in relation to treatment neuronal nicotinic
receptor disorders effect on neurotransmitter release)

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR
THIS RECORD. ALL CITATIONS AVAILABLE IN
THE RE FORMAT

L12 ANSWER 24 OF 45 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1999:457542 HCAPLUS

DOCUMENT NUMBER: 131:211802

TITLE: Functional .alpha.6-containing nicotinic
receptors are present in chick retina

AUTHOR(S): Vailati, Silvia; Hanke, Wolfgang; Bejan,
Andreea; Barabino, Benedetta; Longhi, Renato;
Balestra, Barbara; Moretti, Milena; Clementi,
Francesco; Gotti, Cecilia

CORPORATE SOURCE: Consiglio Nazionale delle Ricerche (CNR)
Cellular and Molecular Pharmacology Center,
Department of Medical Pharmacology, University
of Milan, Milan, Italy

SOURCE: Molecular Pharmacology (1999), 56(1), 11-19

PUBLISHER: CODEN: MOPMA3; ISSN: 0026-895X
American Society for Pharmacology and
Experimental Therapeutics

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Despite the fact that the neuronal chick .alpha.6 subunit was first
cloned several years ago and recently has been shown to form
acetylcholine (ACh)-activated channels in heterologous systems, no
information is yet available concerning the structure and function
of the .alpha.6-contg. nicotinic receptors in neuronal tissues.
Using subunit-specific antibodies directed against 2 different
epitopes of the chick .alpha.6 subunit, we performed immunopptn.
expts. on immunopurified .alpha.6-contg. receptors radiolabeled with
the nicotinic agonist [3H]epibatidine (Epi): almost all of the
.alpha.6 receptors contained the .beta.4 subunit, 51% the .beta.3
subunit, 42% the .alpha.3 subunit, and 7.5% the .beta.2 subunit.
Western blot analyses of the purified receptors confirmed the
presence of the .alpha.3, .beta.3, .beta.2, and .beta.4 subunits,
and the absence of the .alpha.4, .alpha.5, and .alpha.7 subunits.
The .alpha.6-contg. receptors bind [3H]Epi (K_d = 35 pM) and a no. of
other nicotinic agonists with very high affinity, the rank order
being Epi >> cytisine > nicotine > 1,1-dimethyl-4-phenylpiperazinium
> acetylcholine > carbamylcholine. The .alpha.6 receptors also have
a distinct antagonist pharmacol. profile with a rank order of
potency of .alpha.-conotoxin MII > methyllycaconitine >
dihydro-.beta.-erythroidine > MG624 > d-tubocurarine > decamethonium
> hexamethonium. When reconstituted in lipid bilayers, the
.alpha.6-contg. receptors form functional cationic channels with a
main conductance state of 48 pS. These channels are activated by
nicotinic agonists in a dose-dependent manner, and blocked by the
nicotinic antagonist d-tubocurarine.

IT 175735-93-0, .alpha.-Conotoxin MII

RL: BAC (Biological activity or effector, except adverse); BSU

(Biological study, unclassified); BIOL (Biological study)

(functional .alpha.6-contg. nicotinic receptors are present in
chick retina)

REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE
FOR THIS RECORD. ALL CITATIONS AVAILABLE

Searcher : Shears 308-4994

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IN THE RE FORMAT

L12 ANSWER 25 OF 45 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1999:334877 HCAPLUS

DOCUMENT NUMBER: 131:84191

TITLE: Inhibition of nicotine-induced hippocampal norepinephrine release in rats by alpha-conotoxins MII and AuIB microinjected into the locus ceruleus

AUTHOR(S): Fu, Yitong; Matta, Shannon G.; McIntosh, J. Michael; Sharp, Burt M.

CORPORATE SOURCE: Department of Pharmacology, University of Tennessee-Memphis, Memphis, TN, 38163, USA

SOURCE: Neuroscience Letters (1999), 266(2), 113-116

CODEN: NELED5; ISSN: 0304-3940

PUBLISHER: Elsevier Science Ireland Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Hippocampal norepinephrine (NE) is secreted by neurons projecting from the locus ceruleus (LC) to the hippocampus; LC nicotinic receptors (NACHRs) are involved in the effects of systemic nicotine on this pathway. To clarify the NACHR subtypes, NACHR antagonists, termed a-conotoxins, were microinjected into the LC before nicotine; MII and AuIB were used to assess the potential involvement of .alpha.3.beta.2 and .alpha.3.beta.4 subunit-contg. NACHRs, resp. Nicotine dose-dependently stimulated hippocampal NE release ($P < 0.01$); MII (>0.25 pmol) reduced the NE response to nicotine (67% decrease; $P < 0.05$), as did AuIB (44% redn. by 25 pmol; $P < 0.05$). Administered together, however, MII and AuIB were no more effective than MII. Thus, MII and AuIB are capable of interacting with NACHR subtypes other than those previously defined as .alpha.3.beta.2 and .alpha.3.beta.4, resp. NACHRs contg. both .beta.2 and .beta.4 subunits may be involved.

IT 175735-93-0, .alpha.-Conotoxin MII

RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)

(inhibition of nicotine-induced hippocampal norepinephrine release by alpha-conotoxins MII and AuIB microinjected into locus ceruleus)

REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 26 OF 45 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1999:297438 HCAPLUS

DOCUMENT NUMBER: 130:297009

TITLE: Preparation and interaction of .alpha.-conotoxin peptides with neuronal nicotinic acetylcholine receptors

INVENTOR(S): Shon, Ki-joon; Olivera, Baldomero M.; Rivier, Jean E.; Koerber, Steven C.; Shen, Gregory S.; McIntosh, J. Michael; Cartier, G. Edward; Yoshikami, Doju

PATENT ASSIGNEE(S): University of Utah Research Foundation, USA; Case Western Reserve University; Salk Institute; Cognetix, Inc.

SOURCE: PCT Int. Appl., 176 pp.

CODEN: PIXXD2

Searcher : Shears 308-4994

09/897465

DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9921878	A1	19990506	WO 1998-US22368	19981023
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2308115	AA	19990506	CA 1998-2308115	19981023
AU 9911143	A1	19990517	AU 1999-11143	19981023
EP 1032588	A1	20000906	EP 1998-953885	19981023
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2001521042	T2	20011106	JP 2000-517986	19981023
PRIORITY APPLN. INFO.:			US 1997-62783P	P 19971024
			US 1997-65814P	P 19971114
			WO 1998-US22368	W 19981023

OTHER SOURCE(S): MARPAT 130:297009

AB This invention relates to conopeptide MII derivs.
 Xaa-Cys-Cys-Xaa-Xaa1-Xaa2-Xaa-Cys-Xaa3-Xaa-Xaa4-Xaa5-Xaa-Xaa-Cys
 (Xaa = natural, modified, of non-natural amino acid residue;
 modifications may be addn., substitution, or deletion of one or more
 amino acid residues; or include addn. or substitution of amino acid
 analogs; Xaa1 = any amino acid, preferably Asn or His; Xaa2 = any
 amino acid, preferably Pro or Hyp; Xaa3 = any amino acid, preferably
 His or Asn; Xaa4 = any amino acid, preferably Glu; Xaa5 = any amino
 acid, preferably His or Asn) in which amino acid residues are
 substituted as described herein while maintaining the basic activity
 of MII. The present invention also relates to the discovery of the
 3-dimensional structure of MII, and the relationship of its
 structure to its specificity to the .alpha.3.beta.2 subtype of the
 neuronal nicotinic acetylcholine receptor (nAChR). The present
 invention also relates to computer based programs for the expression
 of the three-dimensional structure of MII and peptide analogs,
 peptide mimetics or non-peptide mimetics thereof. The structural
 characteristics may be correlated with biol. activity to enable the
 design of .alpha.-4/7 conotoxin peptide analogs and peptide mimetics
 which demonstrate the same specificity to neuronal nAChR. Such
 analogs and peptide mimetics are useful as cardiovascular agents and
 for treating or detecting small-cell lung carcinoma (SCLC).

IT 175735-93-0P, .alpha.-Conotoxin MII
 RL: BAC (Biological activity or effector, except adverse); BSU
 (Biological study, unclassified); PRP (Properties); SPN (Synthetic
 preparation); THU (Therapeutic use); BIOL (Biological study); PREP
 (Preparation); USES (Uses)
 (prepn. and interaction of .alpha.-conotoxin
 peptides with neuronal nicotinic acetylcholine receptors)
 IT 223416-40-8P 223416-43-1P, .alpha.-
 Conotoxin Au IC 223416-44-2P 223416-45-3P

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223416-46-4P 223416-48-6P 223416-49-7P
223416-50-0P 223416-51-1P 223416-52-2P
223416-53-3P 223416-54-4P 223416-55-5P

RL: BAC (Biological activity or effector, except adverse); BSU
(Biological study, unclassified); SPN (Synthetic preparation); THU
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
(Uses)

(prepn. and interaction of **.alpha.-conotoxin**

peptides with neuronal nicotinic acetylcholine receptors)

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR
THIS RECORD. ALL CITATIONS AVAILABLE IN
THE RE FORMAT

L12 ANSWER 27 OF 45 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1999:275773 HCAPLUS

DOCUMENT NUMBER: 131:69359

TITLE: Identification of tyrosine sulfation in *Conus*
pennaceus conotoxins **.alpha.-PnIA** and
.alpha.-PnIB: further investigation of labile
sulfo- and phosphopeptides by electrospray,
matrix-assisted laser desorption/ionization
(MALDI) and atmospheric pressure MALDI mass
spectrometry

AUTHOR(S): Wolfender, Jean-Luc; Chu, Feixia; Ball, Haydn;
Wolfender, Florence; Fainzilber, Michael;
Baldwin, Michael A.; Burlingame, Alma L.

CORPORATE SOURCE: Department of Pharmaceutical Chemistry and Mass
Spectrometry Facility, University of California,
San Francisco, CA, 94143-0446, USA

SOURCE: Journal of Mass Spectrometry (1999), 34(4),
447-454

CODEN: JMSPFJ; ISSN: 1076-5174

PUBLISHER: John Wiley & Sons Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Liq. chromatog./electrospray ionization mass spectrometry was used
to investigate the peptide compn. of the venom of *Conus pennaceus*, a
molluscivorous cone shell from the Red Sea. Based on obsd. Mrs,
this venom contained all known conotoxins previously isolated and
identified from this species. Interestingly, the doubly protonated
species of only two of these conotoxins, **.alpha.-PnIA** and
.alpha.-PnIB, showed addnl. related ions at +40 m/z (+80 Da),
indicating the presence of either sulfation or phosphorylation in
both components. High-performance liq. chromatog. (HPLC) fractions
contg. these two conotoxins were examd. by matrix-assisted laser
desorption/ionization (MALDI) mass spectrometry in both pos. and
neg. ion modes, as well as by MALDI high-energy collision-induced
dissoecn. These expts. established the presence of a single sulfated
tyrosine residue within both **.alpha.-PnIA** and **.alpha.-PnIB**. Hence
their post-translationally modified sequences are
GCCSLPPCAANNPDY(S)C-NH2 (**.alpha.-PnIA**) and GCCSLPPCALSNDY(S)C-NH2
(**.alpha.-PnIB**). This assignment was supported by comparison of
their mass spectral behavior with that of known sulfated and
phosphorylated peptides. This data clarified further the
distinguishing features of the ionization and fragmentation of such
modified peptides. Selective disulfide folding of synthetic
.alpha.-PnIB demonstrated that both sulfated and non-sulfated toxins
co-elute on reversed-phase HPLC and that **.alpha.-PnIB** possesses the

same disulfide connectivity as other "classical" .alpha.-conotoxins reported previously.

IT 157961-36-9, .alpha.-Conotoxin Pn IA
(reduced) 157998-82-8, .alpha.-Conotoxin
Pn IB (reduced)

RL: ANT (Analyte); BOC (Biological occurrence); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study); OCCU (Occurrence)

(identification of tyrosine sulfation in *Conus pennaceus* conotoxins .alpha.-PnIA and .alpha.-PnIB and investigation of labile sulfo- and phosphopeptides by electrospray, MALDI, and atm. pressure MALDI mass spectrometry)

REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 28 OF 45 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1999:168172 HCAPLUS

DOCUMENT NUMBER: 130:307784

TITLE: NMR Solution Structure of .alpha.-Conotoxin ImI and Comparison to Other Conotoxins Specific for Neuronal Nicotinic Acetylcholine Receptors
AUTHOR(S): Rogers, Jessica P.; Luginbuehl, Peter; Shen, Gregory S.; McCabe, R. Tyler; Stevens, Raymond C.; Wemmer, David E.

CORPORATE SOURCE: Department of Chemistry, University of California, Berkeley, CA, 94720, USA

SOURCE: Biochemistry (1999), 38(13), 3874-3882
CODEN: BICHAW; ISSN: 0006-2960

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB .alpha.-Conotoxins, peptides produced by predatory species of *Conus* marine snails, are potent antagonists of nicotinic acetylcholine receptors (nAChRs), ligand-gated ion channels involved in synaptic transmission. We detd. the NMR soln. structure of the smallest known .alpha.-conotoxin, ImI, a 12 amino acid peptide that binds specifically to neuronal .alpha.7-contg. nAChRs in mammals. Calcn. of the structure was based on a total of 80 upper distance constraints and 31 dihedral angle constraints resulting in 20 representative conformers with an av. pairwise rmsd of 0.44 .ANG. from the mean structure for the backbone atoms N, C.alpha., and C' of residues 2-11. The structure of ImI is characterized by two compact loops, defined by two disulfide bridges, which form distinct subdomains sepd. by a deep cleft. Two short 310-helical regions in the first loop are followed by a C-terminal .beta.-turn in the second. The two disulfide bridges and Ala 9 form a rigid hydrophobic core, orienting the other amino acid side chains toward the surface. Comparison of the three-dimensional structure of ImI to those of the larger, 16 amino acid .alpha.-conotoxins PnIA, PnIB, MII, and EpI-also specific for neuronal nAChRs-reveals remarkable similarity in local backbone conformations and relative solvent-accessible surface areas. The core scaffold is conserved in all five conotoxins, whereas the residues in solvent-exposed positions are highly variable. The second helical region, and the specific amino acids that the helix exposes to solvent, may be particularly important for binding and selectivity. This comparative anal. provides a three-dimensional structural basis for

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interpretation of mutagenesis data and structure-activity relationships for ImI as well other neuronal .alpha.-conotoxins.
IT 175735-93-0, .alpha.-Conotoxin MII
195823-99-5, .alpha.-Conotoxin PnIB
195824-00-1, .alpha.-Conotoxin PnIA
211050-66-7, .alpha.-Conotoxin Epi
RL: PRP (Properties)
(NMR soln. structure of .alpha.-conotoxin ImI and comparison to other conotoxins specific for neuronal nicotinic acetylcholine receptors)
REFERENCE COUNT: 75 THERE ARE 75 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 29 OF 45 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:764295 HCAPLUS
DOCUMENT NUMBER: 130:21651
TITLE: Toxic conopeptides AuIA, AuIB and AuIC of cone snail venom active against nicotinic receptors
INVENTOR(S): McIntosh, J. Michael; Cartier, G. Edward; Yoshikami, Doju; Luo, Siqin; Olivera, Baldomero M.
PATENT ASSIGNEE(S): University of Utah Research Foundation, USA
SOURCE: PCT Int. Appl., 22 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9851322	A1	19981119	WO 1998-US7004	19980409
W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG			
US 5866682	A	19990202	US 1997-857068	19970515
AU 9871043	A1	19981208	AU 1998-71043	19980409
PRIORITY APPLN. INFO.:			US 1997-857068	19970515
			WO 1998-US7004	19980409

OTHER SOURCE(S): MARPAT 130:21651

AB Peptides of 14-17 residues in length that are found in the venom of cone snails or analogs to the naturally available peptides, and which include two cyclizing disulfide linkages are described. These peptides are active against the .alpha.3.beta.4 subtype of the nicotinic acetylcholine receptor. More specifically, the present invention is directed to conopeptides having the general formula: Gly-Cys-Cys-Ser-Tyr-Xaa1-Xaa1-Cys-Phe-Ala-Thr-Asn-Xaa2-Xaa3-Xaa4-Cys, wherein Xaa1 is Pro or Hyp (trans-4-hydroxy-Pro), Xaa2 is Ser, Pro or Hyp, Xaa3 is Gly or Asp and Xaa4 is a Tyr or des- Xaa4. The disulfide bridges are between the first and third between the second fourth cysteine residues. The C-terminal end is preferably

Searcher : Shears 308-4994

amidated. These peptides may be pharmaceutically useful.

IT 216299-20-6, .alpha.-Conotoxin Au IA

223416-43-1, .alpha.-Conotoxin Au IC

RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); OCCU (Occurrence)

(toxic conopeptides AuIA, AuIB and AuIC of cone snail venom active against nicotinic receptors)

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 30 OF 45 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1998:676036 HCAPLUS

DOCUMENT NUMBER: 130:48561

TITLE: Three-Dimensional Solution Structure of .alpha.-Conotoxin MII by NMR Spectroscopy: Effects of Solution Environment on Helicity
AUTHOR(S): Hill, Justine M.; Oomen, Clasien J.; Miranda, Les P.; Bingham, Jon-Paul; Alewood, Paul F.; Craik, David J.

CORPORATE SOURCE: Centre for Drug Design and Development, The University of Queensland, Brisbane, 4072, Australia

SOURCE: Biochemistry (1998), 37(45), 15621-15630

CODEN: BICHAW; ISSN: 0006-2960

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB .alpha.-Conotoxin MII, a 16-residue polypeptide from the venom of the piscivorous cone snail *Conus magus*, is a potent and highly specific blocker of mammalian neuronal nicotinic acetylcholine receptors composed of .alpha.3.beta.2 subunits. The role of this receptor type in the modulation of neurotransmitter release and its relevance to the problems of addiction and psychosis emphasize the importance of a structural understanding of the mode of interaction of MII with the .alpha.3.beta.2 interface. Here we describe the three-dimensional soln. structure of MII detd. using 2D 1H NMR spectroscopy. Structural restraints consisting of 376 interproton distances inferred from NOEs and 12 dihedral restraints derived from spin-spin coupling consts. were used as input for simulated annealing calcns. and energy minimization in the program X-PLOR. The final set of 20 structures is exceptionally well-defined with mean pairwise rms differences over the whole mol. of 0.07 .ANG. for the backbone atoms and 0.34 .ANG. for all heavy atoms. MII adopts a compact structure incorporating a central segment of .alpha.-helix and .beta.-turns at the N- and C-termini. The mol. is stabilized by two disulfide bonds, which provide cross-links between the N-terminus and both the middle and C-terminus of the structure. The susceptibility of the structure to conformational change was examd. using several different solvent conditions. While the global fold of MII remains the same, the structure is stabilized in a more hydrophobic environment provided by the addn. of acetonitrile or trifluoroethanol to the aq. soln. The distribution of amino acid side chains in MII creates distinct hydrophobic and polar patches on its surface that may be important for the specific interaction with the .alpha.3.beta.2 neuronal nAChR. A comparison of the structure

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of MII with other neuronal-specific .alpha.-conotoxins provides insights into their mode of interaction with these receptors.

IT 175735-93-0, .alpha.-Conotoxin MII

RL: PRP (Properties)

(three-dimensional soln. structure of .alpha.-

conotoxin MII by NMR spectroscopy and effects of soln. environment on helicity)

REFERENCE COUNT: 56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 31 OF 45 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1998:475696 HCAPLUS

DOCUMENT NUMBER: 129:226831

TITLE: The 1.1 .ANG. Resolution Crystal Structure of [Tyr15]EpI, a Novel .alpha.-Conotoxin from Conus episcopatus, Solved by Direct Methods

AUTHOR(S): Hu, Shu-Hong; Loughnan, Marion; Miller, Russ; Weeks, Charles M.; Blessing, Robert H.; Alewood, Paul F.; Lewis, Richard J.; Martin, Jennifer L.

CORPORATE SOURCE: Centre for Drug Design and Development, University of Queensland, Brisbane, 4072, Australia

SOURCE: Biochemistry (1998), 37(33), 11425-11433
CODEN: BICHAW; ISSN: 0006-2960

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Conotoxins are valuable probes of receptors and ion channels because of their small size and highly selective activity.

.alpha.-Conotoxin EpI, a 16-residue peptide from the mollusk-hunting Conus episcopatus, has the amino acid sequence

GCCSDPRCNMNNPDY(SO3H)C-NH2 and appears to be an extremely potent and selective inhibitor of the .alpha.3.beta.2 and .alpha.3.beta.4

neuronal subtypes of the nicotinic acetylcholine receptor (nAChR).

The desulfated form of EpI ([Tyr15]EpI) has a potency and selectivity for the nAChR receptor similar to those of EpI. Here we

describe the crystal structure of [Tyr15]EpI solved at a resoln. of 1.1 .ANG. using SnB. The asym. unit has a total of 284 non-hydrogen

atoms, making this one of the largest structures solved de novo by direct methods. The [Tyr15]EpI structure brings to six the no. of

.alpha.-conotoxin structures that have been detd. to date. Four of these, [Tyr15]EpI, PnIA, PnIB, and MII, have an .alpha.4/7 cysteine

framework and are selective for the neuronal subtype of the nAChR. The structure of [Tyr15]EpI has the same backbone fold as the other

.alpha.4/7-conotoxin structures, supporting the notion that this conotoxin cysteine framework and spacing give rise to a conserved

fold. The surface charge distribution of [Tyr15]EpI is similar to that of PnIA and PnIB but is likely to be different from that of

II, suggesting that [Tyr15]EpI and MII may have different binding modes for the same receptor subtype.

IT 212758-79-7

RL: PRP (Properties)

(1.1 .ANG. resoln. crystal structure of [Tyr15]EpI, a novel

.alpha.-conotoxin from Conus episcopatus,

solved by direct methods)

REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE

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IN THE RE FORMAT

L12 ANSWER 32 OF 45 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1998:400592 HCAPLUS

DOCUMENT NUMBER: 129:157855

TITLE: .alpha.-Conotoxin EpI, a novel sulfated peptide from *Conus episcopatus* that selectively targets neuronal nicotinic acetylcholine receptors

AUTHOR(S): Loughnan, Marion; Bond, Trudy; Atkins, Anne; Cuevas, Javier; Adams, David J.; Broxton, Natalie M.; Livett, Bruce G.; Down, John G.; Jones, Alun; Alewood, Paul F.; Lewis, Richard J.

CORPORATE SOURCE: Centre for Drug Design and Development, The University of Queensland, St. Lucia, 4067, Australia

SOURCE: Journal of Biological Chemistry (1998), 273(25), 15667-15674

CODEN: JBCHA3; ISSN: 0021-9258

PUBLISHER: American Society for Biochemistry and Molecular Biology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB We have isolated and characterized .alpha.-conotoxin EpI, a novel sulfated peptide from the venom of the molluscivorous snail, *Conus episcopatus*. The peptide was classified as an .alpha.-conotoxin based on sequence, disulfide connectivity, and pharmacol. target. EpI has homol. to sequences of previously described .alpha.-conotoxins, particularly PnIA, PnIB, and ImI. However, EpI differs from previously reported conotoxins in that it has a sulfotyrosine residue, identified by amino acid anal. and mass spectrometry. Native EpI was shown to coelute with synthetic EpI. The peptide sequence is consistent with most, but not all, recognized criteria for predicting tyrosine sulfation sites in proteins and peptides. The activities of synthetic EpI and its unsulfated analog [Tyr15]EpI were similar. Both peptides caused competitive inhibition of nicotine action on bovine adrenal chromaffin cells (neuronal nicotinic ACh receptors) but had no effect on the rat phrenic nerve-diaphragm (muscle nicotinic ACh receptors). Both EpI and [Tyr15]EpI partly inhibited acetylcholine-evoked currents in isolated parasympathetic neurons of rat intracardiac ganglia. These results indicate that EpI and [Tyr15]EpI selectively inhibit .alpha.3.beta.2 and .alpha.3.beta.4 nicotinic acetylcholine receptors.

IT 211050-66-7P, .alpha.-Conotoxin Ep I

RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); PUR (Purification or recovery); BIOL (Biological study); PREP (Preparation); PROC (Process)

(.alpha.-conotoxin EpI is novel sulfated peptide from *Conus episcopatus* that selectively targets neuronal nicotinic acetylcholine receptors)

REFERENCE COUNT: 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 33 OF 45 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1998:394229 HCAPLUS

DOCUMENT NUMBER: 129:37452

09/897465

TITLE: Use of .alpha.-conotoxin MII? to treat disorders resulting from nicotine-stimulated dopamine release

INVENTOR(S): McIntosh, J. Michael; Kulak, Jennifer M.; Yoshikami, Doju; Olivera, Baldomero M.

PATENT ASSIGNEE(S): University of Utah Research Foundation, USA

SOURCE: PCT Int. Appl., 30 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9824462	A1	19980611	WO 1997-US22350	19971205
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5780433	A	19980714	US 1996-761674	19961206
AU 9856909	A1	19980629	AU 1998-56909	19971205
US 5922679	A	19990713	US 1998-45925	19980323
US 5929034	A	19990727	US 1998-45926	19980323
PRIORITY APPLN. INFO.:			US 1996-761674	19961206
			WO 1997-US22350	19971205
AB Neuronal nicotinic acetylcholine receptors (nAChRs) are believed to mediate nicotine addiction. In addn., stimulation of nAChRs modulates release of neurotransmitters including dopamine, norepinephrine and serotonin. Thus, pharmacol. manipulation of nicotinic receptors has implications for a wide variety of disorders including psychotic, mood, movement and cognitive. For most nAChRs, there are no subtype selective ligands. However, .alpha.-conotoxin MII, a small peptide from the carnivorous marine snail Conus magus, was recently isolated. This peptide has been shown to be a specific antagonist for .alpha.3.beta.2 nicotinic receptors. The peptide potentially blocks part, but not all, of nicotine-stimulated dopamine release from rat brain striatal synaptosomes. In contrast it has no effect on potassium stimulated dopamine release. Other .alpha.-conotoxins specifically target distinct neuronal nAChR subtypes. .alpha.-Conotoxins thus represent new lead compds. for CNS disorders.				
IT 175735-93-0, .alpha.-Conotoxin MII				
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)				
(use of .alpha.-conotoxin MII to treat disorders resulting from nicotine-stimulated dopamine release)				
REFERENCE COUNT:	6	THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT		

L12 ANSWER 34 OF 45 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1998:351777 HCAPLUS

Searcher : Shears 308-4994

09/897465

DOCUMENT NUMBER: 129:12744
 TITLE: Use of conotoxin peptides ImI and MII as cardiovascular agents
 INVENTOR(S): McIntosh, J. Michael; Olivera, Baldomero M.; Yoshikami, Doju
 PATENT ASSIGNEE(S): University of Utah Research Foundation, USA; McIntosh, J. Michael; Olivera, Baldomero M.; Yoshikami, Doju
 SOURCE: PCT Int. Appl., 24 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9822126	A1	19980528	WO 1997-US20669	19971117
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9852555	A1	19980610	AU 1998-52555	19971117
AU 735724	B2	20010712		
EP 948346	A1	19991013	EP 1997-947488	19971117
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2001505878	T2	20010508	JP 1998-523732	19971117
PRIORITY APPLN. INFO.: US 1996-31141P P 19961118				
WO 1997-US20669 W 19971117				
AB	ImI and MII conotoxin peptides, and derivs. thereof, are used as cardiovascular agents including, but not limited to, heart rate-regulating agents, blood pressure-regulating agents and antiarrhythmic agents.			
IT	175735-93-0, .alpha.-Conotoxin M II			
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)				
(conotoxin peptides ImI and MII as cardiovascular agents)				
REFERENCE COUNT:	1	THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT		
L12 ANSWER 35 OF 45 HCAPLUS COPYRIGHT 2003 ACS				
ACCESSION NUMBER:	1998:128874 HCAPLUS			
DOCUMENT NUMBER:	128:240575			
TITLE:	Differential inhibition by .alpha.-conotoxin-MII of the nicotinic stimulation of [3H] dopamine release from rat striatal synaptosomes and slices			
AUTHOR(S):	Kaiser, S. A.; Soliakov, L.; Harvey, S. C.; Luetje, C. W.; Wonnacott, S.			
CORPORATE SOURCE:	Department of Biology and Biochemistry,			

Searcher : Shears 308-4994

09/897465

SOURCE: University of Bath, Bath, BA2 7AY, UK
Journal of Neurochemistry (1998), 70(3),
1069-1076
CODEN: JONRA9; ISSN: 0022-3042
PUBLISHER: Lippincott-Raven Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The presynaptic nicotinic modulation of dopamine release from striatal nerve terminals is well established, but the subtype(s) of neuronal nicotinic acetylcholine receptor (nAChR) underlying this response has not been identified. Recently, .alpha.-conotoxin-MII has been reported to inhibit potently and selectively the rat .alpha.3.beta.2 combination of nAChR subunits. Here we have synthesized the peptide, confirmed its specificity, and examd. its effect on the (.+-.)-anatoxin-a-evoked release of [3H]-dopamine from rat striatal synaptosomes and slices. .alpha.-Conotoxin-MII (112 nM) completely blocked acetylcholine-evoked currents of .alpha.3.beta.2 nAChRs expressed in Xenopus oocytes (IC50 = 8.0.+-.1.1 nM). Pairwise combinations of other nicotinic subunits were not blocked by 112 nM .alpha.-conotoxin-MII. On perfused striatal synaptosomes and slices, .alpha.-conotoxin-MII dose-dependently inhibited [3H]dopamine release evoked by 1 .mu.M (.+-.)-anatoxin-a with IC50 values of 24.3.+-.2.9 and 17.3.+-.0.1 nM, resp. The dose-response curve was shifted to the right with increasing agonist concns. However, the maximal inhibition of responses achieved by .alpha.-conotoxin-MII (112 nM) was 44.9.+-.5.4% for synaptosomes and 25.0.+-.4.1% for slices, compared with an inhibition by 10 .mu.M mecamylamine of 77.9.+-.3.7 and 88.0.+-.2.1%, resp. These results suggest the presence of presynaptic .alpha.3.beta.2-like nAChRs on striatal dopaminergic terminals, but the incomplete block of (.+-.)-anatoxin-a-evoked [3H]dopamine release by .alpha.-conotoxin-MII also supports the participation of nAChRs composed of other subunits. The lower inhibition found in slices is consistent with an addnl. indirect nicotinic stimulation of dopamine release via an .alpha.-conotoxin-MII-insensitive nAChR.

IT 175735-93-0, .alpha.-Conotoxin-MII

RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)

(.alpha.-conotoxin-MII effect on dopamine release from striatal synaptosomes and slices in relation to nicotinic receptors)

L12 ANSWER 36 OF 45 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1998:6399 HCAPLUS

DOCUMENT NUMBER: 128:19563

TITLE: Three-Dimensional Solution Structure of .alpha.-Conotoxin MII, an .alpha.3.beta.2 Neuronal Nicotinic Acetylcholine Receptor-Targeted Ligand

AUTHOR(S): Shon, Ki-Joon; Koerber, Steven C.; Rivier, Jean E.; Olivera, Baldomero M.; McIntosh, J. Michael
CORPORATE SOURCE: Department of Physiology and Biophysics, Case Western Reserve University, Cleveland, OH, 44106, USA

SOURCE: Biochemistry (1997), 36(50), 15693-15700

CODEN: BICHAW; ISSN: 0006-2960

PUBLISHER: American Chemical Society

Searcher : Shears 308-4994

DOCUMENT TYPE: Journal
 LANGUAGE: English

AB The three-dimensional structure of .alpha.-conotoxin MII in aq. soln. has been detd. by two-dimensional 1H NMR spectroscopy. NOE-derived distances, refined by an iterative relaxation matrix approach, as well as dihedral and chirality restraints were used in high-temp. biphasic simulated annealing calcns. Fourteen min. energy structures out of 50 subjected to the SA simulations were chosen for evaluation; these 14 structures have a final RMS deviation of 0.76.+-.0.31 and 1.35.+-.0.34 .ANG. for the backbone and heavy atoms, resp. The overall structure is unusually well-defined due to a large helical component around the two disulfide bridges. The principal backbone folding motif may be common to a subclass of .alpha.-conotoxins. There are two distinct surfaces on the mol. almost at right angles to one another. One entirely consists of the hydrophobic residues Gly1, Cys2, Cys3, Leu15, and Cys16. The second comprises the hydrophilic residues Glu11, His12, Ser13, and Asn14. These surfaces on the ligand could be essential for the subtype-specific recognition of the receptor.

IT 175735-93-0, .alpha.-Conotoxin MII

RL: PRP (Properties)

(three-dimensional soln. structure of .alpha.-conotoxin MII)

L12 ANSWER 37 OF 45 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1997:577191 HCAPLUS

DOCUMENT NUMBER: 127:244160

TITLE: Crystal Structure at 1.1 .ANG. Resolution of .alpha.-Conotoxin PnIB: Comparison with .alpha.-Conotoxins PnIA and GI

AUTHOR(S): Hu, Shu-Hong; Gehrmann, John; Alewood, Paul F.; Craik, David J.; Martin, Jennifer L.

CORPORATE SOURCE: Centre for Drug Design and Development, University of Queensland, Brisbane, 4072, Australia

SOURCE: Biochemistry (1997), 36(38), 11323-11330
 CODEN: BICHAW; ISSN: 0006-2960

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Here, we describe the crystal structure of PnIB, solved at a resolu. of 1.1 .ANG. and phased using the Shake-and-Bake direct methods program. PnIB crystals are orthorhombic and belong to the space group P212121 with the following unit cell dimensions: a = 14.6 .ANG., b = 26.1 .ANG., and c = 29.2 .ANG.. The final refined structure of .alpha.-conotoxin PnIB includes all 16 residues plus 23 solvent mols. and has an overall R-factor of 14.7% (R-free of 15.9%). The crystal structures of the .alpha.-conotoxins PnIB and PnIA are solved from different crystal forms, with different solvent contents. Comparison of the structures reveals them to be very similar, showing that the unique backbone and disulfide architecture is not strongly influenced by crystal lattice constraints or solvent interactions. This finding supports the notion that this structural scaffold is a rigid support for the presentation of important functional groups. The structures of PnIB and PnIA differ in their shape and surface charge distribution from that of GI.

IT 195823-99-5, .alpha.-Conotoxin Pn IB

195824-00-1, .alpha.-Conotoxin Pn IA

09/897465

RL: PRP (Properties)

(crystal structure at 1.1 .ANG. resoln. of .alpha.-
conotoxin PnIB in relation to .alpha.-
conotoxins PnIA and GI)

L12 ANSWER 38 OF 45 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1997:212436 HCAPLUS

DOCUMENT NUMBER: 126:208398

TITLE: Differential block of nicotinic synapses on B
versus C neurons in sympathetic ganglia of frog
by .alpha.-conotoxins MII and ImI

AUTHOR(S): Tavazoie, Sohail F.; Tavazoie, Masoud F.;
Mcintosh, J. Michael; Olivera, Baldomero M.;
Yoshikami, Doju

CORPORATE SOURCE: Department of Biology, University of Utah, Salt
Lake City, UT, 84112, USA

SOURCE: British Journal of Pharmacology (1997), 120(6),
995-1000

CODEN: BJPCBM; ISSN: 0007-1188

PUBLISHER: Stockton

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The effects of two new acetylcholine receptor antagonists,
.alpha.-conotoxin MII and .alpha.-conotoxin ImI, on nicotinic
synaptic transmission in the 10th paravertebral sympathetic ganglion
of the leopard frog (*Rana pipiens*) were examd. The preganglionic
nerve was elec. stimulated (at low frequency, .ltoreq. min-1, to
avoid use-dependent changes) while compd. action potentials of B and
C neurons were monitored from the postganglionic nerve.
.alpha.-Conotoxins MII and ImI, at low micromolar concns.,
reversibly blocked both B and C waves. .alpha.-Conotoxin MII
blocked the C wave more effectively than the B wave, whereas the
potency of .alpha.-conotoxin ImI was opposite that of MII. The
observation that nicotinic antagonists can differentially block
synaptic transmission of B vs. C neurons with opposite selectivities
strongly suggests that these neurons possess distinct nicotinic
receptors. In addn. to fast and slow B waves described by others, C
waves with two temporally distinguishable components were present in
our recordings. Each .alpha.-conotoxin affected fast and slow B
waves similarly. Likewise, toxins did not discriminate between the
two components of C waves. This suggests that all neurons within
each major class (B or C) may have the same nicotinic receptors.
Synthetic forms of .alpha.-conotoxins MII and ImI were used in the
present study. Their ease of synthesis and their specificities
should make these toxins useful probes to investigate the various
subtypes of neuronal nicotinic acetylcholine receptors.

IT 175735-93-0, .alpha.-Conotoxin MII

RL: ADV (Adverse effect, including toxicity); BIOL (Biological
study)

(differential block of nicotinic synapses on B vs. C neurons in
sympathetic ganglia by .alpha.-conotoxins MII
and ImI)

L12 ANSWER 39 OF 45 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1997:131527 HCAPLUS

DOCUMENT NUMBER: 126:234634

TITLE: Determinants of specificity for
.alpha.-conotoxin MII on .alpha.3.beta.2

Searcher : Shears 308-4994

09/897465

AUTHOR(S): neuronal nicotinic receptors
Harvey, Scott C.; McIntosh, J. Michael; Cartier,
G. Edward; Maddox, Floyd N.; Luetje, Charles W.
CORPORATE SOURCE: Department of Molecular and Cellular
Pharmacology, University of Miami School of
Medicine, Miami, FL, 33101, USA
SOURCE: Molecular Pharmacology (1997), 51(2), 336-342
CODEN: MOPMA3; ISSN: 0026-895X
PUBLISHER: Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The competitive antagonist .alpha.-conotoxin-MII (.alpha.-CTx-MII)
is highly selective for the .alpha.3.beta.2 neuronal nicotinic
receptor. Other receptor subunit combinations (.alpha.2.beta.2,
.alpha.4.beta.2, .alpha.3.beta.4) are >200-fold less sensitive to
blockade by this toxin. Using chimeric and mutant subunits, we
identified amino acid residues of .alpha.3 and .beta.2 that
participate in detn. of .alpha.-CTx-MII sensitivity. Chimeric
.alpha. subunits, constructed from the .alpha.3 and .alpha.4
subunits, as well as from the .alpha.3 and .alpha.2 subunits, were
expressed in combination with the .beta.2 subunit in Xenopus laevis
oocytes. Chimeric .beta. subunits, formed from the .beta.2 and
.beta.4 subunits, were expressed in combination with .alpha.3.
Determinants of .alpha.-CTx-MII sensitivity on .alpha.3 were found
to be within sequence segments 121-181 and 181-195. The 181-195
segment accounted for approx. half the difference in toxin
sensitivity between receptors formed by .alpha.2 and .alpha.3. When
this sequence of .alpha.2 was replaced with the corresponding
.alpha.3 sequence, the resulting chimera formed receptors only
26-fold less sensitive to .alpha.-CTx-MII than .alpha.3.beta.2.
Site-directed mutagenesis within segment 181-195 demonstrated that
Lys 185 and Ile188 are crit. in detn. of sensitivity to toxin
blockade. Determinants of .alpha.-CTx-MII sensitivity on .beta.2
were mapped to sequence segments 1-54, 54-63, and 63-80.
Site-directed mutagenesis within segment 54-63 of .beta.2
demonstrated that Thr59 is important in detg. .alpha.-CTx-MII
sensitivity.
IT 175735-93-0, .alpha.-Conotoxin MII
RL: BPR (Biological process); BSU (Biological study, unclassified);
BIOL (Biological study); PROC (Process)
(determinants of specificity for .alpha.-
conotoxin MII on .alpha.3.beta.2 neuronal nicotinic
receptors)
L12 ANSWER 40 OF 45 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1997:124468 HCAPLUS
DOCUMENT NUMBER: 126:126900
TITLE: Use of conotoxin peptides U002 and MII for
treating or detecting small-cell lung carcinoma
INVENTOR(S): Olivera, Baldomera M.; Cruz, Lourdes J.;
Hillyard, David R.; McIntosh, J. Michael;
Santos, Ameurfino S.
PATENT ASSIGNEE(S): University of Utah Research Fondation, USA
SOURCE: PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7

Searcher : Shears 308-4994

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9640211	A1	19961219	WO 1996-US7962	19960604
W: AU, CA, JP				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 5595972	A	19970121	US 1995-487174	19950607
AU 9662503	A1	19961230	AU 1996-62503	19960604
AU 695055	B2	19980806		
EP 844883	A1	19980603	EP 1996-921234	19960604
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 11506737	T2	19990615	JP 1996-500831	19960604
PRIORITY APPLN. INFO.:				
			US 1995-487174	A 19950607
			US 1993-84848	A2 19930629
			US 1993-137800	A2 19931019
			WO 1996-US7962	W 19960604

AB The present invention is directed to use of relatively short peptides, specifically the .alpha.-conotoxin peptides MII and U002, for treating patients with small-cell lung carcinoma (SCLC) or for detecting the presence of SCLC tumors. It has been discovered that while MII and U002 bind to neuronal nicotinic receptors as do other .alpha.-conotoxin peptides, they have a significantly lower affinity for neuromuscular receptors. Patients having SCLC are treated in accordance with the present invention by administering, preferably i.v. or i.m., a pharmaceutical compn. contg. the .alpha.-conotoxin peptide as the active ingredient. The presence or location of SCLC tumors are detected in accordance with the present invention by injecting a subject with MII or U002 labeled with a marker capable of detection and subsequently detecting the binding of the labeled MII or U002 to det. the presence or location of SCLC tumors.

IT **186420-62-2, .alpha.-Conotoxin M II**
(reduced)

RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); USES (Uses)

(.alpha.-conotoxin peptides U002 and MII for treating or detecting small-cell lung carcinoma)

L12 ANSWER 41 OF 45 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1997:85606 HCAPLUS

DOCUMENT NUMBER: 126:152786

TITLE: Conotoxin peptides

INVENTOR(S): Olivera, Baldomero M.; Cruz, Lourdes J.; Hillyard, David R.; McIntosh, J. Michael; Santos, Ameurfino D.

PATENT ASSIGNEE(S): University of Utah Research Foundation, USA

SOURCE: U.S., 35 pp., Cont.-in-part of U.S. 5,514,774.

CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 7

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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Searcher : Shears 308-4994

09/897465

US 5595972	A	19970121	US 1995-487174	19950607
US 5432155	A	19950711	US 1993-84848	19930629
US 5514774	A	19960507	US 1993-137800	19931019
CA 2223737	AA	19961219	CA 1996-2223737	19960604
WO 9640211	A1	19961219	WO 1996-US7962	19960604
W: AU, CA, JP				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9662503	A1	19961230	AU 1996-62503	19960604
AU 695055	B2	19980806		
EP 844883	A1	19980603	EP 1996-921234	19960604
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 11506737	T2	19990615	JP 1996-500831	19960604
PRIORITY APPLN. INFO.:				
			US 1993-84848	A2 19930629
			US 1993-137800	A2 19931019
			US 1995-487174	A 19950607
			WO 1996-US7962	W 19960604

AB The invention is directed to A-lineage conotoxin peptides, which are conotoxin peptides that have strong homol. in the signal sequence and the 3'-untranslated region of the genes coding for these peptides to the sequences in the .alpha.-conotoxin peptides. The A-lineage conotoxin peptides include the .alpha.-conotoxin peptides, the .alpha.-conotoxin-like peptides and the .kappa.-conotoxin peptides, described further below. The .alpha.-conotoxin-peptides generally share a "core" sequence motif. This core sequence is termed the .alpha.3/5 core and is represented as Cys-Cys-Xaa-Xaa-Xaa-Cys-Xaa-Xaa-Xaa-Xaa-Cys (SEQ ID NO: 1). The .alpha.-conotoxin-like peptides generally share a core sequence termed the .alpha.4/7 core and is represented as Cys-Cys-Xaa-Xaa-Xaa-Xaa-Cys-Xaa-Xaa-Xaa-Xaa-Xaa-Cys (SEQ ID NO:2). The .kappa.-conotoxin peptides generally have a core sequence termed the .kappa.7/2/1/3 core and is represented as Cys-Cys-Xaa-Xaa-Xaa-Xaa-Xaa-Xaa-Cys-Xaa-Xaa-Cys-Xaa-Xaa-Xaa-Cys (SEQ ID NO:3); .alpha.-conotoxins MII (SEQ ID NO:54) and U002 (SEQ ID NO:10) preferentially bind to neuronal nicotinic acetylcholine receptors, rather than neuromuscular receptors. These latter two conotoxins can be used to diagnose and treat small-cell lung carcinomas, which have cholinergic nicotinic receptors.

IT 186420-62-2, .alpha.-Conotoxin M II (reduced)

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (.alpha.-conotoxin peptides for use as antitumor agents)

L12 ANSWER 42 OF 45 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1997:34715 HCAPLUS

DOCUMENT NUMBER: 126:182612

TITLE: Identification of genes encoding A-lineage conotoxin peptides by PCR

INVENTOR(S): Olivera, Baldomero M.; Cruz, Lourdes J.; Hillyard, David R.; McIntosh, J. Michael; Santos, Ameurfino D.

PATENT ASSIGNEE(S): University of Utah Research Foundation, USA

SOURCE: U.S., 36 pp., Cont.-in-part of U.S. 5,514,774.

Searcher : Shears 308-4994

09/897465

CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5589340	A	19961231	US 1995-477383	19950607
US 5432155	A	19950711	US 1993-84848	19930629
US 5514774	A	19960507	US 1993-137800	19931019
PRIORITY APPLN. INFO.:			US 1993-84848	A2 19930629
			US 1993-137800	A2 19931019

AB PCR primers for the identification of genes for A-lineage conotoxins are described. A-lineage conotoxin genes are very similar in the signal sequence and the 3'-untranslated region to the genes for .alpha.-conotoxins. The A-lineage conotoxins include the .alpha.-conotoxins, the .alpha.-conotoxin-like peptides and .kappa.-conotoxins. The .alpha.-conotoxin-peptides generally share a "core" sequence motif that is defined by the distribution of cysteines in the minimal biol. active peptide. A no. of novel conotoxins and conotoxin-like peptides are identified. These novel conotoxins may be of therapeutic or investigative use, for example, against tumor cells presenting cholinergic receptors such as small cell lung cancer cells.

IT 186420-62-2, .alpha.-Conotoxin M II
(reduced)

RL: BOC (Biological occurrence); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); OCCU (Occurrence)

(amino acid sequence; process and primers for identifying nucleic acids encoding A-lineage conotoxin peptides)

L12 ANSWER 43 OF 45 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1996:286546 HCAPLUS

DOCUMENT NUMBER: 124:335314

TITLE: The 1.1 .ANG. crystal structure of the neuronal acetylcholine receptor antagonist, .alpha.-conotoxin PnIA from Conus pennaceus
AUTHOR(S): Hu, Shu-Hong; Gehrmann, John; Guddat, Luke W.; Alewood, Paul F.; Craik, David J.; Martin, Jennifer L.

CORPORATE SOURCE: Center Drug Design and Development, Univ. Queensland, St. Lucia, 4072, Australia

SOURCE: Structure (London) (1996), 4(4), 417-423
CODEN: STRUE6; ISSN: 0969-2126

PUBLISHER: Current Biology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The 1.1 .ANG. crystal structure of synthetic PnIA was detd. by direct methods using the Shake-and-Bake program. The three-dimensional structure incorporates a .beta. turn followed by two .alpha.-helical turns. The conformation is stabilized by two disulfide bridges that form the interior of the mol., with all other side chains oriented outwards. The compact architecture of the PnIA toxin provides a rigid framework for presentation of chem. groups that are required for activity. The structure is characterized by distinct hydrophobic and polar surfaces; a 16 .ANG. sepn. of the

Searcher : Shears 308-4994

09/897465

sole pos. and neg. charges (these two charged residues being located at opposite ends of the mol.); a hydrophobic region and a protruding tyrosine side chain. These features may be important for the specific interaction of PnIA with neuronal nAChR.

IT 157961-36-9, .alpha.-Conotoxin Pn IA
(reduced)

RL: PRP (Properties)

(crystal structure of conotoxin PnIA in relation to conformation)

L12 ANSWER 44 OF 45 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1996:198722 HCAPLUS

DOCUMENT NUMBER: 124:281632

TITLE: A new .alpha.-conotoxin which targets
.alpha.3.beta.2 nicotinic acetylcholine
receptors

AUTHOR(S): Cartier, G. Edward; Yoshikami, Doju; Gray,
William R.; Luo, Siqin; Olivera, Baldomero M.;
McIntosh, J. Michael

CORPORATE SOURCE: Dep. Biology, Univ. Utah, Salt Lake City, UT,
84112, USA

SOURCE: Journal of Biological Chemistry (1996), 271(13),
7522-8

PUBLISHER: CODEN: JBCHA3; ISSN: 0021-9258
American Society for Biochemistry and Molecular
Biology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB We have isolated a 16-amino acid peptide from the venom of the
marine snail *Conus magus* which potentially blocks nicotinic
acetylcholine receptors (nAChRs) composed of .alpha.3.beta.2
subunits. This peptide, named .alpha.-conotoxin MII, was identified
by electrophysiol. screening venom fractions against cloned
nicotinic receptors expressed in *Xenopus* oocytes. the peptide's
structure, which has been confirmed by mass spectrometry and total
chem. synthesis, differs significantly from those of all previously
isolated .alpha.-conotoxins. Disulfide bridging, however, is
conserved. The toxin blocks the response to acetylcholine in
oocytes expressing .alpha.3.beta.2 nAChRs with an IC50 of 0.5 nM and
is 2-4 orders of magnitude less potent on other nAChR subunit
combinations. We have recently reported the isolation and
characterization of .alpha.-conotoxin ImI, which selectively targets
homomeric .alpha.7 neuronal nAChRs. Yet other .alpha.-conotoxins
selectively block the muscle subtype of nAChR. Thus, it is
increasingly apparent that .alpha.-conotoxins represent a
significant resource for ligands with which to probe
structure-function relationships of various nAChR subtypes.

IT 175735-93-0P, .alpha.-Conotoxin M II

RL: ADV (Adverse effect, including toxicity); PRP (Properties); PUR
(Purification or recovery); BIOL (Biological study); PREP
(Preparation)

(new .alpha.-conotoxin and targeting of
.alpha.3.beta.2 nicotinic acetylcholine receptors)

L12 ANSWER 45 OF 45 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1994:601190 HCAPLUS

DOCUMENT NUMBER: 121:201190

TITLE: New Mollusk-Specific .alpha.-Conotoxins Block
Aplysia Neuronal Acetylcholine Receptors

Searcher : Shears 308-4994

09/897465

AUTHOR(S): Fainzilber, Michael; Hasson, Arik; Oren, Ruth;
Burlingame, Alma L.; Gordon, Dalia; Spira, Micha
E.; Zlotkin, Eliahu
CORPORATE SOURCE: Silberman Institute of Life Sciences, Hebrew
University of Jerusalem, Jerusalem, 91904,
Israel
SOURCE: Biochemistry (1994), 33(32), 9523-9
CODEN: BICHAW; ISSN: 0006-2960
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Two mollusk-specific neurotoxic peptides from the venom of the
molluscivorous snail *Conus pennaceus* are described. These new
toxins block acetylcholine receptors (AChR) of cultured *Aplysia*
neurons. Bath application of 0.5-1 μ M toxin induces 5-10-mV
membrane depolarization, which recovers to the control level within
1-3 min in the presence of the toxin. This response is blocked by 1
mM hexamethonium. Concomitantly with the transient depolarization,
the toxins block approx. 90% of the depolarizing responses evoked by
brief iontophoretic application of acetylcholine. The pharmacol.
and amino acid sequences of the toxins (.alpha.PnIA,
GCCSLPPCAANNPDYC-NH2; .alpha.PnIB, GCCSLPPCALSNPDYC-NH2) enable
their classification as novel .alpha.-conotoxins. The sequences
differ from those of previously described .alpha.-conotoxins in a no.
of features, the most striking of which is the presence of a single
neg. charged residue in the C-terminal loop. This loop contains a
pos. charged residue in piscivorous venom .alpha.-conotoxins. In
contrast to other .alpha.-conotoxins, which are selective for
vertebrate skeletal muscle nicotinic ACh receptors, these *Conus*
pennaceus toxins block neuronal ACh receptors in molluscs. As such
they are new probes which can be used to define subtypes of ACh
receptors, and they should be useful tools in the study of
structure-function relationships in ACh receptors.

IT 157961-36-9, .alpha.-Conotoxin PnIA
157998-82-8, .alpha.-Conotoxin PnIB

RL: BIOL (Biological study)
(from *Conus pennaceus*, *Aplysia* neuronal acetylcholine receptor
blockage by)

E1 THROUGH E65 ASSIGNED

FILE 'REGISTRY' ENTERED AT 11:33:27 ON 10 JAN 2003

L13 65 SEA FILE=REGISTRY ABB=ON PLU=ON (175735-93-0/BI OR
195823-99-5/BI OR 195824-00-1/BI OR 186420-62-2/BI OR
157961-36-9/BI OR 221639-83-4/BI OR 223416-43-1/BI OR
229639-63-8/BI OR 157998-82-8/BI OR 211050-66-7/BI OR
216299-20-6/BI OR 229639-64-9/BI OR 229639-65-0/BI OR
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Searcher : Shears 308-4994

09/897465

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263028-77-9/BI OR 263028-78-0/BI OR 263028-79-1/BI OR
263028-80-4/BI OR 263028-81-5/BI OR 263028-82-6/BI OR
263028-83-7/BI OR 263028-84-8/BI OR 285558-22-7/BI OR
285558-23-8/BI OR 285558-24-9/BI OR 467428-30-4/BI OR
467428-33-7/BI)

L14 65 L13 AND L1

L14 ANSWER 1 OF 65 REGISTRY COPYRIGHT 2003 ACS

RN 467428-33-7 REGISTRY

CN L-Cysteinamide, glycyl-L-cysteinyl-L-cysteinyl-L-seryl-L-histidyl-L-prolyl-L-alanyl-L-cysteinyl-L-tyrosyl-L-alanyl-L-asparaginyl-L-asparaginyl-L-glutaminy-L-.alpha.-aspartyl-L-tyrosyl- (9CI) (CA INDEX NAME)

OTHER NAMES:

CN 9: PN: WO02079236 SEQID: 9 claimed protein
SQL 16

SEQ 1 GCCSHPCYA NNQDYC
=====

HITS AT: 2-16

REFERENCE 1: 137:289027

L14 ANSWER 2 OF 65 REGISTRY COPYRIGHT 2003 ACS

RN 467428-30-4 REGISTRY

CN L-Cysteinamide, glycyl-L-cysteinyl-L-cysteinyl-L-seryl-L-.alpha.-aspartyl-L-prolyl-L-arginyl-L-cysteinyl-L-asparaginyl-L-tyrosyl-L-.alpha.-aspartyl-L-histidyl-L-prolyl-L-.alpha.-glutamyl-L-isoleucyl- (9CI) (CA INDEX NAME)

OTHER NAMES:

CN 2: PN: WO02079236 SEQID: 2 claimed protein
SQL 16

SEQ 1 GCCSDPRCNY DHPEIC
=====

HITS AT: 2-16

REFERENCE 1: 137:289027

L14 ANSWER 3 OF 65 REGISTRY COPYRIGHT 2003 ACS

RN 285558-24-9 REGISTRY

CN L-Cysteine, L-cysteinyl-L-cysteinyl-L-seryl-L-tyrosyl-L-prolyl-L-prolyl-L-cysteinyl-L-asparaginyl-L-valyl-L-seryl-L-tyrosyl-L-prolyl-L-.alpha.-glutamyl-L-isoleucyl- (9CI) (CA INDEX NAME)

SQL 15

SEQ 1 CCSYPPCNVS YPEIC
=====

HITS AT: 1-15

REFERENCE 1: 133:131093

L14 ANSWER 4 OF 65 REGISTRY COPYRIGHT 2003 ACS

RN 285558-23-8 REGISTRY

CN L-Cysteine, glycylglycyl-L-cysteinyl-L-cysteinyl-L-seryl-L-tyrosyl-L-prolyl-L-prolyl-L-cysteinyl-L-asparaginyl-L-valyl-L-seryl-L-tyrosyl-

09/897465

SQL 17 L-prolyl-L-.alpha.-glutamyl-L-isoleucyl- (9CI) (CA INDEX NAME)

SEQ 1 GGCCSYPPCN VSYPEIC

=====

HITS AT: 3-17

REFERENCE 1: 133:131093

L14 ANSWER 5 OF 65 REGISTRY COPYRIGHT 2003 ACS

RN 285558-22-7 REGISTRY

CN L-Cysteine, L-arginyl-L-alanyl-L-cysteinyl-L-cysteinyl-L-seryl-L-tyrosyl-L-prolyl-L-prolyl-L-cysteinyl-L-asparaginyl-L-valyl-L-asparaginyl-L-tyrosyl-L-prolyl-L-.alpha.-glutamyl-L-isoleucyl- (9CI)

SQL 17

SEQ 1 RACCSYPPCN VNYPEIC

=====

HITS AT: 3-17

REFERENCE 1: 133:131093

L14 ANSWER 6 OF 65 REGISTRY COPYRIGHT 2003 ACS

RN 263028-84-8 REGISTRY

CN L-Cysteinamide, glycyl-L-cysteinyl-L-cysteinyl-L-seryl-L-seryl-L-prolyl-L-prolyl-L-cysteinyl-L-alanyl-L-leucyl-L-asparaginyl-L-asparaginyl-L-prolyl-L-.alpha.-aspartyl-L-tyrosyl-, cyclic (2.fwdarw.8), (3.fwdarw.16)-bis(disulfide) (9CI) (CA INDEX NAME)

SQL 16

SEQ 1 GCCSSPPCAL NNPDYC

=====

HITS AT: 2-16

REFERENCE 1: 132:246458

L14 ANSWER 7 OF 65 REGISTRY COPYRIGHT 2003 ACS

RN 263028-83-7 REGISTRY

CN L-Cysteinamide, glycyl-L-cysteinyl-L-cysteinyl-L-seryl-L-leucyl-L-prolyl-L-prolyl-L-cysteinyl-L-alanyl-L-valyl-L-asparaginyl-L-asparaginyl-L-prolyl-L-.alpha.-aspartyl-L-tyrosyl-, cyclic (2.fwdarw.8), (3.fwdarw.16)-bis(disulfide) (9CI) (CA INDEX NAME)

SQL 16

SEQ 1 GCCSLPPCAV NNPDYC

=====

HITS AT: 2-16

REFERENCE 1: 132:246458

L14 ANSWER 8 OF 65 REGISTRY COPYRIGHT 2003 ACS

RN 263028-82-6 REGISTRY

CN L-Cysteinamide, glycyl-L-cysteinyl-L-cysteinyl-L-seryl-L-leucyl-L-prolyl-L-prolyl-L-cysteinyl-L-alanyl-L-norleucyl-L-asparaginyl-L-asparaginyl-L-prolyl-L-.alpha.-aspartyl-L-tyrosyl-, cyclic (2.fwdarw.8), (3.fwdarw.16)-bis(disulfide) (9CI) (CA INDEX NAME)

SQL 16

09/897465

SEQ 1 GCCSLPPCAX NNPDYC
=====

HITS AT: 2-16

REFERENCE 1: 132:246458

L14 ANSWER 9 OF 65 REGISTRY COPYRIGHT 2003 ACS
RN 263028-81-5 REGISTRY
CN L-Cysteinamide, glycyl-L-cysteiny-L-cysteiny-L-seryl-L-leucyl-L-prolyl-L-prolyl-L-cysteiny-L-alanyl-L-isoleucyl-L-asparaginy-L-asparaginy-L-prolyl-L-.alpha.-aspartyl-L-tyrosyl-, cyclic (2.fwdarw.8), (3.fwdarw.16)-bis(disulfide) (9CI) (CA INDEX NAME)
SQL 16

SEQ 1 GCCSLPPCAI NNPDYC
=====

HITS AT: 2-16

REFERENCE 1: 132:246458

L14 ANSWER 10 OF 65 REGISTRY COPYRIGHT 2003 ACS
RN 263028-80-4 REGISTRY
CN L-Cysteinamide, glycyl-L-cysteiny-L-cysteiny-L-seryl-L-leucyl-L-prolyl-L-prolyl-L-cysteiny-L-alanyl-L-methionyl-L-asparaginy-L-asparaginy-L-prolyl-L-.alpha.-aspartyl-L-tyrosyl-, cyclic (2.fwdarw.8), (3.fwdarw.16)-bis(disulfide) (9CI) (CA INDEX NAME)
SQL 16

SEQ 1 GCCSLPPCAM NNPDYC
=====

HITS AT: 2-16

REFERENCE 1: 132:246458

L14 ANSWER 11 OF 65 REGISTRY COPYRIGHT 2003 ACS
RN 263028-79-1 REGISTRY
CN L-Cysteinamide, glycyl-L-cysteiny-L-cysteiny-L-alanyl-L-alanyl-L-prolyl-L-prolyl-L-cysteiny-L-leucyl-L-leucyl-L-seryl-L-asparaginy-L-prolyl-L-.alpha.-aspartyl-L-tyrosyl-, cyclic (2.fwdarw.8), (3.fwdarw.16)-bis(disulfide) (9CI) (CA INDEX NAME)
SQL 16

SEQ 1 GCCAAPPCLL SNPDYC
=====

HITS AT: 2-16

REFERENCE 1: 132:246458

L14 ANSWER 12 OF 65 REGISTRY COPYRIGHT 2003 ACS
RN 263028-78-0 REGISTRY
CN L-Cysteinamide, glycyl-L-cysteiny-L-cysteiny-L-seryl-L-alanyl-L-prolyl-L-prolyl-L-cysteiny-L-leucyl-L-leucyl-L-seryl-L-asparaginy-L-prolyl-L-.alpha.-aspartyl-L-tyrosyl-, cyclic (2.fwdarw.8), (3.fwdarw.16)-bis(disulfide) (9CI) (CA INDEX NAME)
SQL 16

SEQ 1 GCCSAPPCLL SNPDYC

Searcher : Shears 308-4994

09/897465

=====

HITS AT: 2-16

REFERENCE 1: 132:246458

L14 ANSWER 13 OF 65 REGISTRY COPYRIGHT 2003 ACS
RN 263028-77-9 REGISTRY
CN L-Cysteinamide, glycyl-L-cysteinyl-L-cysteinyl-L-alanyl-L-alanyl-L-prolyl-L-prolyl-L-cysteinyl-L-alanyl-L-leucyl-L-seryl-L-asparaginyl-L-prolyl-L-.alpha.-aspartyl-L-tyrosyl-, cyclic (2.fwdarw.8), (3.fwdarw.16)-bis(disulfide) (9CI) (CA INDEX NAME)
SQL 16

SEQ 1 GCCAAPPCAL SNPDYC

=====

HITS AT: 2-16

REFERENCE 1: 132:246458

L14 ANSWER 14 OF 65 REGISTRY COPYRIGHT 2003 ACS
RN 263028-76-8 REGISTRY
CN L-Cysteinamide, glycyl-L-cysteinyl-L-cysteinyl-L-seryl-L-leucyl-L-prolyl-L-prolyl-L-cysteinyl-L-alanyl-L-leucyl-L-seryl-L-asparaginyl-L-prolyl-L-.alpha.-aspartyl-L-threonyl-, cyclic (2.fwdarw.8), (3.fwdarw.16)-bis(disulfide) (9CI) (CA INDEX NAME)
SQL 16

SEQ 1 GCCSLPPCAL SNPDTCT

=====

HITS AT: 2-16

REFERENCE 1: 132:246458

L14 ANSWER 15 OF 65 REGISTRY COPYRIGHT 2003 ACS
RN 263028-75-7 REGISTRY
CN L-Cysteinamide, glycyl-L-cysteinyl-L-cysteinyl-L-seryl-L-leucyl-L-prolyl-L-prolyl-L-cysteinyl-L-alanyl-L-leucyl-L-seryl-L-asparaginyl-L-prolyl-L-.alpha.-aspartyl-L-alanyl-, cyclic (2.fwdarw.8), (3.fwdarw.16)-bis(disulfide) (9CI) (CA INDEX NAME)
SQL 16

SEQ 1 GCCSLPPCAL SNPDAC

=====

HITS AT: 2-16

REFERENCE 1: 132:246458

L14 ANSWER 16 OF 65 REGISTRY COPYRIGHT 2003 ACS
RN 263028-74-6 REGISTRY
CN L-Cysteinamide, glycyl-L-cysteinyl-L-cysteinyl-L-seryl-L-leucyl-L-prolyl-L-prolyl-L-cysteinyl-L-alanyl-L-leucyl-L-seryl-L-asparaginyl-L-prolyl-L-alanyl-L-tyrosyl-, cyclic (2.fwdarw.8), (3.fwdarw.16)-bis(disulfide) (9CI) (CA INDEX NAME)
SQL 16

SEQ 1 GCCSLPPCAL SNPAYC

=====

HITS AT: 2-16

Searcher : Shears 308-4994

09/897465

REFERENCE 1: 132:246458

L14 ANSWER 17 OF 65 REGISTRY COPYRIGHT 2003 ACS
RN 263028-73-5 REGISTRY
CN L-Cysteinamide, glycyl-L-cysteinyl-L-cysteinyl-L-seryl-L-leucyl-L-prolyl-L-prolyl-L-cysteinyl-L-alanyl-L-leucyl-L-seryl-L-asparaginyl-L-prolyl-L-asparaginyl-L-tyrosyl-, cyclic (2.fwdarw.8), (3.fwdarw.16)-bis(disulfide) (9CI) (CA INDEX NAME)
SQL 16

SEQ 1 GCCSLPPCAL SNPNYC
=====

HITS AT: 2-16

REFERENCE 1: 132:246458

L14 ANSWER 18 OF 65 REGISTRY COPYRIGHT 2003 ACS
RN 263028-72-4 REGISTRY
CN L-Cysteinamide, glycyl-L-cysteinyl-L-cysteinyl-L-seryl-L-leucyl-L-prolyl-L-prolyl-L-cysteinyl-L-alanyl-L-leucyl-L-seryl-L-asparaginyl-3-hydroxy-L-prolyl-L-.alpha.-aspartyl-L-tyrosyl-, cyclic (2.fwdarw.8), (3.fwdarw.16)-bis(disulfide) (9CI) (CA INDEX NAME)
SQL 16

SEQ 1 GCCSLPPCAL SNPDYC
=====

HITS AT: 2-16

RELATED SEQUENCES AVAILABLE WITH SEQLINK

REFERENCE 1: 132:246458

L14 ANSWER 19 OF 65 REGISTRY COPYRIGHT 2003 ACS
RN 263028-71-3 REGISTRY
CN L-Cysteinamide, glycyl-L-cysteinyl-L-cysteinyl-L-seryl-L-leucyl-L-prolyl-L-prolyl-L-cysteinyl-L-alanyl-L-leucyl-L-seryl-L-.alpha.-aspartyl-L-prolyl-L-.alpha.-aspartyl-L-tyrosyl-, cyclic (2.fwdarw.8), (3.fwdarw.16)-bis(disulfide) (9CI) (CA INDEX NAME)
SQL 16

SEQ 1 GCCSLPPCAL SDPDYC
=====

HITS AT: 2-16

REFERENCE 1: 132:246458

L14 ANSWER 20 OF 65 REGISTRY COPYRIGHT 2003 ACS
RN 263028-70-2 REGISTRY
CN L-Cysteinamide, glycyl-L-cysteinyl-L-cysteinyl-L-seryl-L-leucyl-L-prolyl-L-prolyl-L-cysteinyl-L-alanyl-L-leucyl-L-seryl-L-glutaminy-L-prolyl-L-.alpha.-aspartyl-L-tyrosyl-, cyclic (2.fwdarw.8), (3.fwdarw.16)-bis(disulfide) (9CI) (CA INDEX NAME)
SQL 16

SEQ 1 GCCSLPPCAL SQPDYC
=====

HITS AT: 2-16

Searcher : Shears 308-4994

09/897465

REFERENCE 1: 132:246458

L14 ANSWER 21 OF 65 REGISTRY COPYRIGHT 2003 ACS
RN 263028-69-9 REGISTRY
CN L-Cysteinamide, glycyl-L-cysteinyl-L-cysteinyl-L-seryl-L-leucyl-L-prolyl-L-prolyl-L-cysteinyl-L-alanyl-L-leucyl-L-seryl-L-alanyl-L-prolyl-L-.alpha.-aspartyl-L-tyrosyl-, cyclic
(2.fwdarw.8), (3.fwdarw.16)-bis(disulfide) (9CI) (CA INDEX NAME)
SQL 16

SEQ 1 GCCSLPPCAL SAPDYC
=====

HITS AT: 2-16

REFERENCE 1: 132:246458

L14 ANSWER 22 OF 65 REGISTRY COPYRIGHT 2003 ACS
RN 263028-68-8 REGISTRY
CN L-Cysteinamide, glycyl-L-cysteinyl-L-cysteinyl-L-seryl-L-leucyl-L-prolyl-L-prolyl-L-cysteinyl-L-alanyl-L-leucyl-L-alanyl-L-asparaginyl-L-prolyl-L-.alpha.-aspartyl-L-tyrosyl-, cyclic
(2.fwdarw.8), (3.fwdarw.16)-bis(disulfide) (9CI) (CA INDEX NAME)
SQL 16

SEQ 1 GCCSLPPCAL ANPDYC
=====

HITS AT: 2-16

REFERENCE 1: 132:246458

L14 ANSWER 23 OF 65 REGISTRY COPYRIGHT 2003 ACS
RN 263028-67-7 REGISTRY
CN L-Cysteinamide, glycyl-L-cysteinyl-L-cysteinyl-L-seryl-L-leucyl-L-prolyl-L-prolyl-L-cysteinyl-L-alanyl-L-leucyl-L-leucyl-L-asparaginyl-L-prolyl-L-.alpha.-aspartyl-L-tyrosyl-, cyclic
(2.fwdarw.8), (3.fwdarw.16)-bis(disulfide) (9CI) (CA INDEX NAME)
SQL 16

SEQ 1 GCCSLPPCAL LNPDYC
=====

HITS AT: 2-16

REFERENCE 1: 132:246458

L14 ANSWER 24 OF 65 REGISTRY COPYRIGHT 2003 ACS
RN 263028-66-6 REGISTRY
CN L-Cysteinamide, glycyl-L-cysteinyl-L-cysteinyl-L-seryl-L-leucyl-L-prolyl-L-prolyl-L-cysteinyl-L-alanyl-L-tryptophyl-L-seryl-L-asparaginyl-L-prolyl-L-.alpha.-aspartyl-L-tyrosyl-, cyclic
(2.fwdarw.8), (3.fwdarw.16)-bis(disulfide) (9CI) (CA INDEX NAME)
SQL 16

SEQ 1 GCCSLPPCAW SNPDYC
=====

HITS AT: 2-16

REFERENCE 1: 132:246458

Searcher : Shears 308-4994

L14 ANSWER 25 OF 65 REGISTRY COPYRIGHT 2003 ACS
RN 263028-65-5 REGISTRY
CN L-Cysteinamide, glycyl-L-cysteinyl-L-cysteinyl-L-seryl-L-leucyl-L-prolyl-L-prolyl-L-cysteinyl-L-leucyl-L-leucyl-L-seryl-L-asparaginyl-L-prolyl-L-.alpha.-aspartyl-L-tyrosyl-, cyclic
(2.fwdarw.8), (3.fwdarw.16)-bis(disulfide) (9CI) (CA INDEX NAME)
SQL 16

SEQ 1 GCCSLPPCLL SNPDYC
=====

HITS AT: 2-16

REFERENCE 1: 132:246458

L14 ANSWER 26 OF 65 REGISTRY COPYRIGHT 2003 ACS
RN 263028-64-4 REGISTRY
CN L-Cysteinamide, glycyl-L-cysteinyl-L-cysteinyl-L-seryl-L-leucyl-L-prolyl-L-prolyl-L-cysteinyl-L-seryl-L-leucyl-L-seryl-L-asparaginyl-L-prolyl-L-.alpha.-aspartyl-L-tyrosyl-, cyclic
(2.fwdarw.8), (3.fwdarw.16)-bis(disulfide) (9CI) (CA INDEX NAME)
SQL 16

SEQ 1 GCCSLPPCSL SNPDYC
=====

HITS AT: 2-16

REFERENCE 1: 132:246458

L14 ANSWER 27 OF 65 REGISTRY COPYRIGHT 2003 ACS
RN 263028-63-3 REGISTRY
CN L-Cysteinamide, glycyl-L-cysteinyl-L-cysteinyl-L-seryl-L-leucyl-L-prolyl-L-prolyl-L-cysteinylglycyl-L-leucyl-L-seryl-L-asparaginyl-L-prolyl-L-.alpha.-aspartyl-L-tyrosyl-, cyclic
(2.fwdarw.8), (3.fwdarw.16)-bis(disulfide) (9CI) (CA INDEX NAME)
SQL 16

SEQ 1 GCCSLPPCGL SNPDYC
=====

HITS AT: 2-16

REFERENCE 1: 132:246458

L14 ANSWER 28 OF 65 REGISTRY COPYRIGHT 2003 ACS
RN 263028-62-2 REGISTRY
CN L-Cysteinamide, glycyl-L-cysteinyl-L-cysteinyl-L-seryl-L-leucyl-L-prolyl-(4R)-4-hydroxy-L-prolyl-L-cysteinyl-L-alanyl-L-leucyl-L-seryl-L-asparaginyl-L-prolyl-L-.alpha.-aspartyl-L-tyrosyl-, cyclic
(2.fwdarw.8), (3.fwdarw.16)-bis(disulfide) (9CI) (CA INDEX NAME)
SQL 16

SEQ 1 GCCSLPXCAL SNPDYC
=====

HITS AT: 2-16

REFERENCE 1: 132:246458

L14 ANSWER 29 OF 65 REGISTRY COPYRIGHT 2003 ACS

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RN 263028-61-1 REGISTRY
CN L-Cysteinamide, glycyl-L-cysteinyl-L-cysteinyl-L-seryl-L-leucyl-L-prolyl-3-hydroxy-L-prolyl-L-cysteinyl-L-alanyl-L-leucyl-L-seryl-L-asparaginyl-L-prolyl-L-.alpha.-aspartyl-L-tyrosyl-, cyclic
(2.fwdarw.8), (3.fwdarw.16)-bis(disulfide) (9CI) (CA INDEX NAME)
SQL 16

SEQ 1 GCCSLPPCAL SNPDYC
=====

HITS AT: 2-16

RELATED SEQUENCES AVAILABLE WITH SEQLINK

REFERENCE 1: 132:246458

L14 ANSWER 30 OF 65 REGISTRY COPYRIGHT 2003 ACS
RN 263028-59-7 REGISTRY
CN L-Cysteinamide, glycyl-L-cysteinyl-L-cysteinyl-L-seryl-L-leucyl-3-hydroxy-L-prolyl-L-prolyl-L-cysteinyl-L-alanyl-L-leucyl-L-seryl-L-asparaginyl-L-prolyl-L-.alpha.-aspartyl-L-tyrosyl-, cyclic
(2.fwdarw.8), (3.fwdarw.16)-bis(disulfide) (9CI) (CA INDEX NAME)
SQL 16

SEQ 1 GCCSLPPCAL SNPDYC
=====

HITS AT: 2-16

RELATED SEQUENCES AVAILABLE WITH SEQLINK

REFERENCE 1: 132:246458

L14 ANSWER 31 OF 65 REGISTRY COPYRIGHT 2003 ACS
RN 263028-58-6 REGISTRY
CN L-Cysteinamide, glycyl-L-cysteinyl-L-cysteinyl-L-seryl-L-seryl-L-prolyl-L-prolyl-L-cysteinyl-L-alanyl-L-leucyl-L-seryl-L-asparaginyl-L-prolyl-L-.alpha.-aspartyl-L-tyrosyl-, cyclic
(2.fwdarw.8), (3.fwdarw.16)-bis(disulfide) (9CI) (CA INDEX NAME)
SQL 16

SEQ 1 GCCSSPPCAL SNPDYC
=====

HITS AT: 2-16

REFERENCE 1: 132:246458

L14 ANSWER 32 OF 65 REGISTRY COPYRIGHT 2003 ACS
RN 263028-57-5 REGISTRY
CN L-Cysteinamide, glycyl-L-cysteinyl-L-cysteinyl-L-seryl-L-alanyl-L-prolyl-L-prolyl-L-cysteinyl-L-alanyl-L-leucyl-L-seryl-L-asparaginyl-L-prolyl-L-.alpha.-aspartyl-L-tyrosyl-, cyclic
(2.fwdarw.8), (3.fwdarw.16)-bis(disulfide) (9CI) (CA INDEX NAME)
SQL 16

SEQ 1 GCCSAPPCAL SNPDYC
=====

HITS AT: 2-16

REFERENCE 1: 132:246458

Searcher : Shears 308-4994

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L14 ANSWER 33 OF 65 REGISTRY COPYRIGHT 2003 ACS
RN 263028-56-4 REGISTRY
CN L-Cysteinamide, glycyl-L-cysteinyl-L-cysteinyl-L-leucyl-L-leucyl-L-prolyl-L-prolyl-L-cysteinyl-L-alanyl-L-leucyl-L-seryl-L-asparaginyl-L-prolyl-L-.alpha.-aspartyl-L-tyrosyl-, cyclic
(2.fwdarw.8), (3.fwdarw.16)-bis(disulfide) (9CI) (CA INDEX NAME)
SQL 16

SEQ 1 GCCLLPPCAL SNPDYC
=====

HITS AT: 2-16

REFERENCE 1: 132:246458

L14 ANSWER 34 OF 65 REGISTRY COPYRIGHT 2003 ACS
RN 263028-55-3 REGISTRY
CN L-Cysteinamide, glycyl-L-cysteinyl-L-cysteinyl-L-alanyl-L-leucyl-L-prolyl-L-prolyl-L-cysteinyl-L-alanyl-L-leucyl-L-seryl-L-asparaginyl-L-prolyl-L-.alpha.-aspartyl-L-tyrosyl-, cyclic
(2.fwdarw.8), (3.fwdarw.16)-bis(disulfide) (9CI) (CA INDEX NAME)
SQL 16

SEQ 1 GCCALPPCAL SNPDYC
=====

HITS AT: 2-16

REFERENCE 1: 132:246458

L14 ANSWER 35 OF 65 REGISTRY COPYRIGHT 2003 ACS
RN 263028-54-2 REGISTRY
CN L-Cysteinamide, L-glutaminy-L-cysteinyl-L-cysteinyl-L-seryl-L-leucyl-L-prolyl-L-prolyl-L-cysteinyl-L-alanyl-L-leucyl-L-seryl-L-asparaginyl-L-prolyl-L-.alpha.-aspartyl-L-tyrosyl-, cyclic
(2.fwdarw.8), (3.fwdarw.16)-bis(disulfide) (9CI) (CA INDEX NAME)
SQL 16

SEQ 1 QCCSLPPCAL SNPDYC
=====

HITS AT: 2-16

REFERENCE 1: 132:246458

L14 ANSWER 36 OF 65 REGISTRY COPYRIGHT 2003 ACS
RN 263028-53-1 REGISTRY
CN L-Cysteinamide, N-acetylglycyl-L-cysteinyl-L-cysteinyl-L-seryl-L-leucyl-L-prolyl-L-prolyl-L-cysteinyl-L-alanyl-L-leucyl-L-seryl-L-asparaginyl-L-prolyl-L-.alpha.-aspartyl-L-tyrosyl-, cyclic
(2.fwdarw.8), (3.fwdarw.16)-bis(disulfide) (9CI) (CA INDEX NAME)
SQL 16

SEQ 1 GCCSLPPCAL SNPDYC
=====

HITS AT: 2-16

RELATED SEQUENCES AVAILABLE WITH SEQLINK

REFERENCE 1: 132:246458

Searcher : Shears 308-4994

09/897465

L14 ANSWER 37 OF 65 REGISTRY COPYRIGHT 2003 ACS
RN 229639-65-0 REGISTRY
CN L-Cysteinamide, 3,5-diiodo-L-tyrosylglycyl-L-cysteiny-L-cysteiny-L-seryl-L-asparaginy-L-prolyl-L-valyl-L-cysteiny-L-histidyl-L-leucyl-L-.alpha.-glutamyl-L-histidyl-L-seryl-L-asparaginy-L-leucyl- (9CI)
(CA INDEX NAME)

SQL 17

SEQ 1 YGCCSNPVCH LEHSNLC
=====

HITS AT: 3-17

RELATED SEQUENCES AVAILABLE WITH SEQLINK

REFERENCE 1: 131:82983

L14 ANSWER 38 OF 65 REGISTRY COPYRIGHT 2003 ACS
RN 229639-64-9 REGISTRY
CN L-Cysteinamide, 3-iodo-L-tyrosylglycyl-L-cysteiny-L-cysteiny-L-seryl-L-asparaginy-L-prolyl-L-valyl-L-cysteiny-L-histidyl-L-leucyl-L-.alpha.-glutamyl-L-histidyl-L-seryl-L-asparaginy-L-leucyl- (9CI)
(CA INDEX NAME)

SQL 17

SEQ 1 YGCCSNPVCH LEHSNLC
=====

HITS AT: 3-17

RELATED SEQUENCES AVAILABLE WITH SEQLINK

REFERENCE 1: 131:82983

L14 ANSWER 39 OF 65 REGISTRY COPYRIGHT 2003 ACS
RN 229639-63-8 REGISTRY
CN L-Cysteinamide, glycyl-L-cysteiny-L-cysteiny-L-seryl-L-leucyl-L-prolyl-L-prolyl-L-cysteiny-L-alanyl-L-alanyl-L-seryl-L-asparaginy-L-prolyl-L-.alpha.-aspartyl-L-tyrosyl-, cyclic
(2.fwdarw.8), (3.fwdarw.16)-bis(disulfide) (9CI) (CA INDEX NAME)

SQL 16

SEQ 1 GCCSLPPCAA SNPDYC
=====

HITS AT: 2-16

REFERENCE 1: 132:246458

REFERENCE 2: 132:132466

REFERENCE 3: 131:82983

L14 ANSWER 40 OF 65 REGISTRY COPYRIGHT 2003 ACS
RN 229639-62-7 REGISTRY
CN L-Cysteinamide, L-tyrosylglycyl-L-cysteiny-L-cysteiny-L-seryl-L-tyrosyl-L-prolyl-L-prolyl-L-cysteiny-L-phenylalanyl-L-alanyl-L-threonyl-L-asparaginy-L-seryl-L-.alpha.-aspartyl-L-tyrosyl-, cyclic
(3.fwdarw.9), (4.fwdarw.17)-bis(disulfide) (9CI) (CA INDEX NAME)

SQL 17

Searcher : Shears 308-4994

09/897465

SEQ 1 YGCCSYPPCF ATNSDYC
=====

HITS AT: 3-17

REFERENCE 1: 131:82983

L14 ANSWER 41 OF 65 REGISTRY COPYRIGHT 2003 ACS
RN 229639-61-6 REGISTRY
CN L-Cysteinamide, glycyl-L-cysteinyl-L-cysteinyl-L-seryl-L-asparaginyl-L-prolyl-L-valyl-L-cysteinyl-L-phenylalanyl-L-alanyl-L-threonyl-L-histidyl-L-seryl-L-asparaginyl-L-leucyl-, cyclic
(2.fwdarw.8), (3.fwdarw.16)-bis(disulfide) (9CI) (CA INDEX NAME)
SQL 16

SEQ 1 GCCSNPVCFA THSNLC
=====

HITS AT: 2-16

REFERENCE 1: 131:82983

L14 ANSWER 42 OF 65 REGISTRY COPYRIGHT 2003 ACS
RN 229639-60-5 REGISTRY
CN L-Cysteinamide, L-tyrosylglycyl-L-cysteinyl-L-cysteinyl-L-seryl-L-asparaginyl-L-prolyl-L-valyl-L-cysteinyl-L-histidyl-L-leucyl-L-.alpha.-glutamyl-L-histidyl-L-seryl-L-asparaginyl-L-leucyl-, cyclic
(3.fwdarw.9), (4.fwdarw.17)-bis(disulfide) (9CI) (CA INDEX NAME)
SQL 17

SEQ 1 YGCCSNPVCH LEHSNLC
=====

HITS AT: 3-17

RELATED SEQUENCES AVAILABLE WITH SEQLINK

REFERENCE 1: 131:82983

L14 ANSWER 43 OF 65 REGISTRY COPYRIGHT 2003 ACS
RN 223416-55-5 REGISTRY
CN .alpha.-Conotoxin M II, 15-L-alanine- (9CI) (CA INDEX NAME)
SQL 16

SEQ 1 GCCSNPVCHL EHSNAC
=====

HITS AT: 2-16

REFERENCE 1: 130:297009

L14 ANSWER 44 OF 65 REGISTRY COPYRIGHT 2003 ACS
RN 223416-54-4 REGISTRY
CN .alpha.-Conotoxin M II, 14-L-alanine- (9CI) (CA INDEX NAME)
SQL 16

SEQ 1 GCCSNPVCHL EHSALC
=====

HITS AT: 2-16

REFERENCE 1: 130:297009

Searcher : Shears 308-4994

09/897465

L14 ANSWER 45 OF 65 REGISTRY COPYRIGHT 2003 ACS
RN 223416-53-3 REGISTRY
CN .alpha.-Conotoxin M II, 13-L-alanine- (9CI) (CA INDEX NAME)
SQL 16

SEQ 1 GCCSNPVCHL EHANLC
=====

HITS AT: 2-16

REFERENCE 1: 130:297009

L14 ANSWER 46 OF 65 REGISTRY COPYRIGHT 2003 ACS
RN 223416-52-2 REGISTRY
CN .alpha.-Conotoxin M II, 12-L-alanine- (9CI) (CA INDEX NAME)
SQL 16

SEQ 1 GCCSNPVCHL EASNLC
=====

HITS AT: 2-16

REFERENCE 1: 130:297009

L14 ANSWER 47 OF 65 REGISTRY COPYRIGHT 2003 ACS
RN 223416-51-1 REGISTRY
CN .alpha.-Conotoxin M II, 11-L-alanine- (9CI) (CA INDEX NAME)
SQL 16

SEQ 1 GCCSNPVCHL AHSNLC
=====

HITS AT: 2-16

REFERENCE 1: 130:297009

L14 ANSWER 48 OF 65 REGISTRY COPYRIGHT 2003 ACS
RN 223416-50-0 REGISTRY
CN .alpha.-Conotoxin M II, 10-L-alanine- (9CI) (CA INDEX NAME)
SQL 16

SEQ 1 GCCSNPVCHA EHSNLC
=====

HITS AT: 2-16

REFERENCE 1: 130:297009

L14 ANSWER 49 OF 65 REGISTRY COPYRIGHT 2003 ACS
RN 223416-49-7 REGISTRY
CN .alpha.-Conotoxin M II, 9-L-alanine- (9CI) (CA INDEX NAME)
SQL 16

SEQ 1 GCCSNPVCAL EHSNLC
=====

HITS AT: 2-16

REFERENCE 1: 130:297009

L14 ANSWER 50 OF 65 REGISTRY COPYRIGHT 2003 ACS
RN 223416-48-6 REGISTRY

Searcher : Shears 308-4994

09/897465

CN .alpha.-Conotoxin M II, 7-L-alanine- (9CI) (CA INDEX NAME)
SQL 16

SEQ 1 GCCSNPACHL EHSNLC
=====

HITS AT: 2-16

REFERENCE 1: 130:297009

L14 ANSWER 51 OF 65 REGISTRY COPYRIGHT 2003 ACS
RN 223416-46-4 REGISTRY
CN .alpha.-Conotoxin M II, 5-L-alanine- (9CI) (CA INDEX NAME)
SQL 16

SEQ 1 GCCSAPVCHL EHSNLC
=====

HITS AT: 2-16

REFERENCE 1: 130:297009

L14 ANSWER 52 OF 65 REGISTRY COPYRIGHT 2003 ACS
RN 223416-45-3 REGISTRY
CN .alpha.-Conotoxin M II, 4-L-alanine- (9CI) (CA INDEX NAME)
SQL 16

SEQ 1 GCCANPVCHL EHSNLC
=====

HITS AT: 2-16

REFERENCE 1: 130:297009

L14 ANSWER 53 OF 65 REGISTRY COPYRIGHT 2003 ACS
RN 223416-44-2 REGISTRY
CN .alpha.-Conotoxin M II, 1-L-alanine- (9CI) (CA INDEX NAME)
SQL 16

SEQ 1 ACCSNPVCHL EHSNLC
=====

HITS AT: 2-16

REFERENCE 1: 130:297009

L14 ANSWER 54 OF 65 REGISTRY COPYRIGHT 2003 ACS
RN 223416-43-1 REGISTRY
CN .alpha.-Conotoxin Au IC (9CI) (CA INDEX NAME)
OTHER NAMES:
CN L-Cysteinamide, glycyl-L-cysteinyl-L-cysteinyl-L-seryl-L-tyrosyl-L-
prolyl-L-prolyl-L-cysteinyl-L-phenylalanyl-L-alanyl-L-threonyl-L-
asparaginyll-L-serylglycyl-L-tyrosyl-, cyclic
(2.fwdarw.8), (3.fwdarw.16)-bis(disulfide)
SQL 16

SEQ 1 GCCSYPPCFA TNSGYC
=====

HITS AT: 2-16

REFERENCE 1: 131:82983

Searcher : Shears 308-4994

09/897465

REFERENCE 2: 130:297009

REFERENCE 3: 130:21651

L14 ANSWER 55 OF 65 REGISTRY COPYRIGHT 2003 ACS
RN 223416-40-8 REGISTRY
CN L-Cysteinamide, glycyl-L-cysteinyl-L-cysteinyl-L-seryl-L-asparaginyl-L-prolyl-L-valyl-L-cysteinyl-L-phenylalanyl-L-alanyl-L-threonyl-L-asparaginyl-L-seryl-L-leucyl-L-asparaginyl-, cyclic
(2.fwdarw.8), (3.fwdarw.16)-bis(disulfide) (9CI) (CA INDEX NAME)
SQL 16

SEQ 1 GCCSNPVCFA TNSLNC
=====

HITS AT: 2-16

REFERENCE 1: 130:297009

L14 ANSWER 56 OF 65 REGISTRY COPYRIGHT 2003 ACS
RN 221639-83-4 REGISTRY
CN .alpha.-Conotoxin Pn IA, 10-L-leucine-15-desulfo- (9CI) (CA INDEX NAME)
SQL 16

SEQ 1 GCCSLPPCAL NNPDYC
=====

HITS AT: 1-16

RELATED SEQUENCES AVAILABLE WITH SEQLINK

REFERENCE 1: 132:246458

REFERENCE 2: 132:132466

REFERENCE 3: 131:82983

REFERENCE 4: 130:267767

L14 ANSWER 57 OF 65 REGISTRY COPYRIGHT 2003 ACS
RN 216299-20-6 REGISTRY
CN .alpha.-Conotoxin Au IA (9CI) (CA INDEX NAME)
OTHER NAMES:

CN L-Cysteinamide, glycyl-L-cysteinyl-L-cysteinyl-L-seryl-L-tyrosyl-L-prolyl-L-prolyl-L-cysteinyl-L-phenylalanyl-L-alanyl-L-threonyl-L-asparaginyl-L-seryl-L-.alpha.-aspartyl-L-tyrosyl-, cyclic
(2.fwdarw.8), (3.fwdarw.16)-bis(disulfide)
SQL 16

SEQ 1 GCCSYPPCFA TNSDYC
=====

HITS AT: 2-16

REFERENCE 1: 131:82983

REFERENCE 2: 130:21651

L14 ANSWER 58 OF 65 REGISTRY COPYRIGHT 2003 ACS
RN 212758-79-7 REGISTRY

Searcher : Shears 308-4994

09/897465

CN .alpha.-Conotoxin Ep I, 15-desulfo- (9CI) (CA INDEX NAME)
SQL 16

SEQ 1 GCCSDPRCNM NNPDYC
=====

HITS AT: 2-16

RELATED SEQUENCES AVAILABLE WITH SEQLINK

REFERENCE 1: 129:226831

L14 ANSWER 59 OF 65 REGISTRY COPYRIGHT 2003 ACS
RN 211050-66-7 REGISTRY

CN .alpha.-Conotoxin Ep I (9CI) (CA INDEX NAME)
OTHER NAMES:

CN L-Cysteinamide, glycyl-L-cysteiny-L-cysteiny-L-seryl-L-.alpha.-
aspartyl-L-prolyl-L-arginyl-L-cysteiny-L-asparaginy-L-methionyl-L-
asparaginy-L-asparaginy-L-prolyl-L-.alpha.-aspartyl-O-sulfo-L-
tyrosyl-, cyclic (2.fwdarw.8), (3.fwdarw.16)-bis(disulfide)
SQL 16

SEQ 1 GCCSDPRCNM NNPDYC
=====

HITS AT: 2-16

RELATED SEQUENCES AVAILABLE WITH SEQLINK

REFERENCE 1: 130:307784

REFERENCE 2: 129:157855

L14 ANSWER 60 OF 65 REGISTRY COPYRIGHT 2003 ACS
RN 195824-00-1 REGISTRY

CN .alpha.-Conotoxin Pn IA (9CI) (CA INDEX NAME)
OTHER NAMES:

CN L-Cysteinamide, glycyl-L-cysteiny-L-cysteiny-L-seryl-L-leucyl-L-
prolyl-L-prolyl-L-cysteiny-L-alanyl-L-alanyl-L-asparaginy-L-
asparaginy-L-prolyl-L-.alpha.-aspartyl-O-sulfo-L-tyrosyl-, cyclic
(2.fwdarw.8), (3.fwdarw.16)-bis(disulfide)
SQL 16

SEQ 1 GCCSLPPCAA NNPDYC
=====

HITS AT: 2-16

RELATED SEQUENCES AVAILABLE WITH SEQLINK

REFERENCE 1: 132:318808

REFERENCE 2: 132:246458

REFERENCE 3: 132:237373

REFERENCE 4: 132:132466

REFERENCE 5: 132:9825

REFERENCE 6: 131:82983

Searcher : Shears 308-4994

09/897465

REFERENCE 7: 130:307784

REFERENCE 8: 127:244160

L14 ANSWER 61 OF 65 REGISTRY COPYRIGHT 2003 ACS

RN 195823-99-5 REGISTRY

CN .alpha.-Conotoxin Pn IB (9CI) (CA INDEX NAME)

OTHER NAMES:

CN L-Cysteinamide, glycyl-L-cysteinyl-L-cysteinyl-L-seryl-L-leucyl-L-prolyl-L-prolyl-L-cysteinyl-L-alanyl-L-leucyl-L-seryl-L-asparaginyll-prolyl-L.alpha.-aspartyl-O-sulfo-L-tyrosyl-, cyclic (2.fwdarw.8), (3.fwdarw.16)-bis(disulfide)

SQL 16

SEQ 1 GCCSLPPCAL SNPDYC

=====

HITS AT: 2-16

RELATED SEQUENCES AVAILABLE WITH SEQLINK

REFERENCE 1: 132:318808

REFERENCE 2: 132:246458

REFERENCE 3: 132:237373

REFERENCE 4: 132:132466

REFERENCE 5: 132:9825

REFERENCE 6: 131:82983

REFERENCE 7: 130:307784

REFERENCE 8: 127:244160

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RN 186420-62-2 REGISTRY

CN .alpha.-Conotoxin M II (reduced) (9CI) (CA INDEX NAME)

SQL 16

SEQ 1 GCCSNPVCHL EHSNLC

=====

HITS AT: 2-16

RELATED SEQUENCES AVAILABLE WITH SEQLINK

REFERENCE 1: 126:182612

REFERENCE 2: 126:152786

REFERENCE 3: 126:126900

L14 ANSWER 63 OF 65 REGISTRY COPYRIGHT 2003 ACS

RN 175735-93-0 REGISTRY

CN .alpha.-Conotoxin M II (9CI) (CA INDEX NAME)

OTHER NAMES:

Searcher : Shears 308-4994

09/897465

CN L-Cysteinamide, glycyl-L-cysteinyl-L-cysteinyl-L-seryl-L-asparaginyl-L-prolyl-L-valyl-L-cysteinyl-L-histidyl-L-leucyl-L-.alpha.-glutamyl-L-histidyl-L-seryl-L-asparaginyl-L-leucyl-, cyclic
(2.fwdarw.8), (3.fwdarw.16)-bis(disulfide)

SQL 16

SEQ 1 GCCSNPVCHL EHSNLC

=====

HITS AT: 2-16

RELATED SEQUENCES AVAILABLE WITH SEQLINK

REFERENCE 1: 138:540

REFERENCE 2: 137:273401

REFERENCE 3: 137:226853

REFERENCE 4: 137:76110

REFERENCE 5: 137:59609

REFERENCE 6: 136:396263

REFERENCE 7: 136:273496

REFERENCE 8: 136:65411

REFERENCE 9: 135:271222

REFERENCE 10: 135:137700

L14 ANSWER 64 OF 65 REGISTRY COPYRIGHT 2003 ACS

RN 157998-82-8 REGISTRY

CN .alpha.-Conotoxin Pn IB (reduced) (9CI) (CA INDEX NAME)

OTHER NAMES:

CN L-Cysteinamide, glycyl-L-cysteinyl-L-cysteinyl-L-seryl-L-leucyl-L-prolyl-L-prolyl-L-cysteinyl-L-alanyl-L-leucyl-L-seryl-L-asparaginyl-L-prolyl-L-.alpha.-aspartyl-O-sulfo-L-tyrosyl-

SQL 16

SEQ 1 GCCSLPPCAL SNPDYC

=====

HITS AT: 2-16

RELATED SEQUENCES AVAILABLE WITH SEQLINK

REFERENCE 1: 131:69359

REFERENCE 2: 121:201190

L14 ANSWER 65 OF 65 REGISTRY COPYRIGHT 2003 ACS

RN 157961-36-9 REGISTRY

CN .alpha.-Conotoxin Pn IA (reduced) (9CI) (CA INDEX NAME)

OTHER NAMES:

CN L-Cysteinamide, glycyl-L-cysteinyl-L-cysteinyl-L-seryl-L-leucyl-L-prolyl-L-prolyl-L-cysteinyl-L-alanyl-L-alanyl-L-asparaginyl-L-asparaginyl-L-prolyl-L-.alpha.-aspartyl-O-sulfo-L-tyrosyl-

Searcher : Shears 308-4994

09/897465

SQL 16

SEQ 1 GCCSLPPCAA NNPDYC

HITS AT: 2-16

RELATED SEQUENCES AVAILABLE WITH SEQLINK

REFERENCE 1: 131:69359

REFERENCE 2: 124:335314

REFERENCE 3: 121:201190

FILE 'HOME' ENTERED AT 11:34:18 ON 10 JAN 2003

Searcher : Shears 308-4994